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=> file uspatall
FILE 'USPATFULL' ENTERED AT 13:14:56 ON 18 MAR 2010
CA INDEXING COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPATOLD' ENTERED AT 13:14:56 ON 18 MAR 2010
CA INDEXING COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 13:14:56 ON 18 MAR 2010
CA INDEXING COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)

=> d stat que L24
L1        24050 SEA CARRAGEENAN
L12         253 SEA L1 (5A) (SHELL? OR COAT?)
L13         236 SEA L12 AND (?CELLULOS? OR ?POLYVINYL?)
L14          74 SEA L13 AND PRD<20010928
L15          67 SEA L13 AND PD<20010928
L16          92 SEA L13 AND AD<20010928
L17         127 SEA (L14 OR L15 OR L16)
L18          72 SEA L17 AND PHARM?/BI
L19          59 SEA L18 AND RELEAS?
L22        3862 SEA L1 (3A) 1##
L23        2398 SEA L1 (3A) 2##
L24          25 SEA (L22 OR L23) AND L19


=> d stat que L32
L8           235 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  ?CARRAGEENAN?/CNS
L26           76 SEA L8 (2W) (SHELL? OR COAT?)/IT
L27           14 SEA L26 AND GELLAN GUM?/BI,IT
L28            3 SEA L27 AND PRD<20010928
L29            3 SEA L27 AND PD<20010928
```

```
L30           3 SEA L27 AND AD<20010928
L31           5 SEA (L28 OR L29 OR L30)
L32           3 SEA L31 AND PHARM?


=> d stat que L45
L1        24050 SEA CARRAGEENAN
L12         253 SEA L1 (5A) (SHELL? OR COAT?)
L13         236 SEA L12 AND (?CELLULOS? OR ?POLYVINYL?)
L14          74 SEA L13 AND PRD<20010928
L15          67 SEA L13 AND PD<20010928
L16          92 SEA L13 AND AD<20010928
L17         127 SEA (L14 OR L15 OR L16)
L44         128 SEA L13 AND (PRD<20010929 OR PD<20010929 OR AD<20010929)
L45           1 SEA L44 NOT L17


=> d stat que L42
L8          235 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  ?CARRAGEENAN?/CNS
L26          76 SEA L8 (2W) (SHELL? OR COAT?)/IT
L37          27 SEA L26 AND AD<20010929
L38          23 SEA L26 AND PD<20010929
L39          24 SEA L26 AND PRD<20010929
L40          37 SEA (L37 OR L38 OR L39)
L41          17 SEA L40 AND PHARM?/BI,IT
L42          17 SEA L41 AND (?CELLULOS? OR ?POLYVINYL?)/BI,IT


=> d stat que L51
L1        24050 SEA CARRAGEENAN
L12         253 SEA L1 (5A) (SHELL? OR COAT?)
L13         236 SEA L12 AND (?CELLULOS? OR ?POLYVINYL?)
L14          74 SEA L13 AND PRD<20010928
L15          67 SEA L13 AND PD<20010928
L16          92 SEA L13 AND AD<20010928
L17         127 SEA (L14 OR L15 OR L16)
L47          35 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  ?GELLAN GUM?/CNS
L48        1027 SEA L47
L49        4175 SEA ?GELLAN GUM?/BI,IT
L50        4269 SEA (L48 OR L49)
L51          11 SEA L17 AND L50


=> d stat que L52
L8          235 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  ?CARRAGEENAN?/CNS
L26          76 SEA L8 (2W) (SHELL? OR COAT?)/IT
L37          27 SEA L26 AND AD<20010929
L38          23 SEA L26 AND PD<20010929
L39          24 SEA L26 AND PRD<20010929
L40          37 SEA (L37 OR L38 OR L39)
L41          17 SEA L40 AND PHARM?/BI,IT
L42          17 SEA L41 AND (?CELLULOS? OR ?POLYVINYL?)/BI,IT
L47          35 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  ?GELLAN GUM?/CNS
L48        1027 SEA L47
L49        4175 SEA ?GELLAN GUM?/BI,IT
L50        4269 SEA (L48 OR L49)
L52           3 SEA L42 AND L50
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=>

=> d stat que L19
L1         24050 SEA CARRAGEENAN
L12          253 SEA L1 (5A) (SHELL? OR COAT?)
L13          236 SEA L12 AND (?CELLULOS? OR ?POLYVINYL?)
L14           74 SEA L13 AND PRD<20010928
L15           67 SEA L13 AND PD<20010928
L16           92 SEA L13 AND AD<20010928
L17          127 SEA (L14 OR L15 OR L16)
L18           72 SEA L17 AND PHARM?/BI
L19           59 SEA L18 AND RELEAS?


=> s L24 or L32 or L45 or L42 or L51 or L52 or L19
L57          79 L24 OR L32 OR L45 OR L42 OR L51 OR L52 OR L19

=> d hitrn 1
```

L57 ANSWER 3 OF 79 USPATFULL on STN
IT **9000-07-1**, Carrageenan
(dip **coating** compns. containing **cellulose** ethers for capsules and tablets)

=> d ibib abs kwic hitrn L57 1-79

L57 ANSWER 1 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2009:102649 USPATFULL
TITLE: METHOD OF DIP-COATING DOSAGE FORMS
INVENTOR(S): GRUBAN, Cyprian, Lansdale, PA, UNITED STATES
Gowan, JR., Walter G., Woodstock, GA, UNITED STATES
Sirpenski, Christopher, Marlton, NJ, UNITED STATES
Papalia, Michelle, Philadelphia, PA, UNITED STATES
Chen, Jen-Chi, Morrisville, PA, UNITED STATES
Bartuli, Frank J., Randolph, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20090092739	A1	20090409
APPLICATION INFO.:	US 2009-335089	A1	20081215 (12)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2002-162653, filed on 15 Apr 2002, PENDING Continuation-in-part of Ser. No. US 2001-812991, filed on 12 Apr 2001, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-291127P	20010515 (60) <--
	US 2001-325726P	20010928 (60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PHILIP S. JOHNSON, JOHNSON & JOHNSON, ONE JOHNSON &
JOHNSON PLAZA, NEW BRUNSWICK, NJ, 08933-7003, US
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
LINE COUNT: 1503
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Water soluble, gelatin-free dip coatings for tablets and capsules comprising sorbose, glycerin and pectin or a combination of pectin and/or tapioca dextrin or comprising hydroxypropyl starch, thickener, and plasticizer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . (OTC) drugs. The ability to combine capsule halves having different colors provides manufacturers with a unique means of distinguishing various **pharmaceutical** products. Many patients preferred capsules over tablets, perceiving them as being easier to swallow. Thus consumers preferred prompted **pharmaceutical** manufacturers to market such products in capsule form even when they were also available in tablet form.

SUMM . . . alternative to capsule products are caplets, which are solid, oblong tablets that are often coated with various polymers such as **cellulose** ethers to improve their aesthetics, stability, and swallowability. Typically, such polymers are applied to the tablets either from solution in . . .

SUMM However, the use of gelatin as a **pharmaceutical** coating material presents certain disadvantages and limitations including the potential for decreased dissolution rate after extended storage due to cross-linking.

SUMM . . . shells via conventional dip molding processing. See also U.S. Pat. No. 4,001,233 (capsules prepared via pan dip coating with

L57 ANSWER 1 OF 79 USPATFULL on STN (Continued)
DETD . . . such as alginates, agar, guar gum, locust bean gum, kappa carrageenan, lota carrageenan, tara, gum arabic, tragacanth, pectin, xanthan gum, **gellan gum**, maltodextrin, galactomannan, pusstulan, laminarin, scleroglucan, gum arabic, inulin, pectin, whelan, chamsan, neoplan, methylan, elsinan, commercially available cellulose gum, gelling starches such. . .

DETD Any plasticizer known in the **pharmaceutical** art is suitable for use in the present invention, and may include, but not be limited to polyethylene glycol, glycerin, . . . gums and mixtures thereof. Suitable sugar-alcohols include sorbitol, mannitol, xylitol, maltitol, erythritol, lactitol, and mixtures thereof. In solutions containing a **cellulose** ether film former, an optional plasticizer may be present in an amount, based upon the total weight of the solution, of . . .

DETD In embodiments wherein a **cellulose** ether film former is used in the composition, the film forming composition for dip coating substrates may

be substantially free. . . .

DETD . . . than about 100 percent, e.g. from about 95 percent to about 99.5 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; and from about 0.5 percent to about 5 percent of a thickener such as a hydrocolloid, e.g., xanthan gum.

DETD . . . is a chemically modified starch, the thickener may be selected from the group consisting of sago, karaya gum, tragacanth gum, konjac, **gellan gum**, agar, gelling starch and derivatives and mixtures thereof.

DETD . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and is substantially free of hydrocolloids, i.e., e.g. contains less than about 0.01% of hydrocolloids.

DETD . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; and from about 0.1 percent to about 1.0 percent, e.g. from about 0.25 percent to about 0.5 percent of a. . .

DETD . . . to about 90 percent, or from about 80 percent to about 90 percent of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, from about 1 percent to about 80 percent, e.g. from about 5 percent to about 50 percent or from about. . .

. . . percent to about 15 percent or from about 10 percent to about 14 percent, of a film former such as **hydroxypropylmethylcellulose** and from about 0.05 percent to about 2 percent, e.g. from about 0.08 percent to about 0.16 percent or from. . .

DETD . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**

DETD . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and is substantially free of hydrocolloids, i.e., e.g. contains less than about 1%, or less than about 9.01% of hydrocolloids.

DETD . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.001 percent to about

L57 ANSWER 1 OF 79 USPATFULL on STN (Continued)
thermoplast **methylcellulose** ether compounds). However, due to potential tampering concerns, hard gelatin capsules are no longer a preferred delivery system for consumer over-the-counter **pharmaceuticals**, dietary supplements, or other such products. Additionally, the properties of an ideal composition into which steel pins are to be. . . .

SUMM b) a thickener selected from the group consisting of kappa carrageenan, iota carrageenan, maltodextrin, **gellan gum**, agar, gelling starch, and derivatives and mixtures thereof; and c) a plasticizer,

DETD . . . parts water required to dissolve 1 part by weight polymeric, water soluble solute. See Remington, "The Science and Practice of Pharmacy," pages 308-309 (20th Ed. 2000). Water is not herein in connection with polymeric materials, shall mean that the polymer swells in.

DETD Dimethicone is a well known **pharmaceutical** material consisting of linear siloxane polymers containing repeat unit of the formula [--(CH.sub.3).sub.2SiO.sub.n stabilized with trimethylsiloxy end blocking units of. . .

DETD . . . via a dip molding process. One composition comprises, consists of, and/or consists essentially of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; and a thickener, such as a hydrocolloid, e.g., xanthan gum or carrageenan. In another embodiment, the composition comprises, consists of, . . . and/or consists essentially of a film former such as hydroxypropyl starch, a thickener selected from kappa or iota carrageenan, maltodextrin, **gellan gum**, agar, gelling starches, and derivatives and mixtures thereof; and a plasticizer. In yet another embodiment, the composition comprises, consists of, and/or consists essentially of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; and optionally a plasticizer, such as vegetable oils, e.g., castor oil; and may optionally be substantially free of thickeners such. . . gum. In yet another embodiment, the composition comprises, consists of, and/or consists essentially of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; an extender, such as polydextrose, e.g., maltodextrin; and optionally a plasticizer, such as glycols, e.g., polyethylene glycol; and may optionally. . . .

DETD . . . use in film forming composition of the present invention. Examples of such film formers include, but are not limited to, **polyvinylalcohol** (PVA), hydroxypropyl starch, hydroxyethyl starch, pullulan, methylethyl starch, carboxymethyl starch, **methylcellulose**, **hydroxypropylcellulose** (HPC), **hydroxyethylcellulose** (HEMC), **hydroxypropylmethylcellulose** (HPMC), **hydroxyethylmethylcellulose** (HEMC), **hydroxyethylethylcellulose** (HEEC), hydroxyethylhydroxypropylmethyl **cellulose** (HEMHPC), methacrylic acid copolymers, methacrylate ester copolymers, **polyvinyl** alcohol and polyethylene glycol copolymers, proteins such as whey protein, egg albumin, casein, zein isolates, soy protein and soy protein. . . .

DETD One suitable **hydroxypropylmethylcellulose** compound is "HPMC 2910", which is a **cellulose** ether having a degree of substitution of about 1.9 and a hydroxypropyl molar substitution of about 0.23. Also containing, based upon.

DETD One suitable **polyvinyl** alcohol and polyethylene glycol copolymer is commercially available from BASF Corporation under the tradename "Kollicoat IR".

L57 ANSWER 1 OF 79 USPATFULL on STN (Continued)
0.1 percent, e.g. from about 0.01 percent to about 0.09 percent of a.

DETD . . . to about 19 percent or from about 16 percent to about 19 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, from about 0.1 percent to about 17 percent, e.g. from about 1 percent to about 11 percent or from about. . .

DETD . . . opacifying agents such as titanium dioxide, and/or from about 0

percent to about 14 percent colorants. See Remington's Practice of **Pharmacy**, Martin & Cook, 17 h ed., pp. 1628-30, which is herein

incorporated by reference.

DETD Any coloring agent suitable for use in **pharmaceutical** applications may be used in the present invention and is preferably water soluble, but not limited to azo dyes, quinophalone dyes,

DETD In one embodiment, the **pharmaceutical** dosage form is comprised of a) a core containing an active ingredient; b) an optional first coating layer

comprised of. . . .

DETD . . . and 6,274,162, which are all incorporated by reference herein. Additional suitable subcoatings include one or more of the following ingredients: **cellulose** ether such as **hydroxypropylcellulose**, **hydroxypropylcellulose**, and **hydroxyethylcellulose**; polysaccharides such as xanthan gum, tragacanth, and alginates; polyalkylenepolyols including for example, glycerin, polyethylene glycol, propylene glycol, diethyl sebecate, triethyl

DETD . . . from about 2 percent to about 8 percent, e.g. from about 4 percent to about 6 percent of a water-soluble **cellulose** ether from about 0.1 percent to about 1 percent, castor oil, as disclosed in detail

in U.S. Pat. No. .

DETD In one embodiment, the film former is a **cellulose** ether such as HPMC, and the thickener is a hydrocolloid such as xanthan gum and the weight gain enhancer is. . . .

DETD . . . any material that can be carried by or entrained in the system.

For example, the active agent can be a **pharmaceutical**, nutraceutical, vitamin, dietary supplement, nutrient, food, foodstuff, dyestuff, nutritional, mineral, supplement, flavoring agent, dye, the like and combinations thereof.

DETD . . . methenamine mandelate; methenyl; meperidine hydrochloride; metaproterenol sulfate; methaqualone and its nitrates; methicrain and its maleate; methyl nicotinate; methyl salicylate; methyl **cellulose**; methsuximide; metoclopramide and its halides/hydrates; metronidazole; metoprotol tartrate; miconazole nitrate; minoxidil; minocycli; morphine; naproxen and its alkali metal sodium . . . of active drugs on a magnesium trisilicate base and on a magnesium aluminum

silicate base, and mixtures thereof. Mixtures and **pharmaceutically** acceptable salts of these and other actives can be used.

DETD In one embodiment, the dosage forms coated with the dip coatings of the present invention provided for immediate **release** of the active ingredient, i.e. the dissolution of the dosage form conformed to USP specifications for immediate **release** tablets containing the particular active ingredient employed. For example, for acetaminophen tablets, USP

L57 ANSWER 1 OF 79 USPATFULL on STN (Continued)
24 specifies that at pH 5.8 phosphate, . . . using USP apparatus 2 [paddles] at 50 rpm, at least 80% of the acetaminophen contained in the dosage form is **released** therefrom within 30 minutes after dosing, and for ibuprofen tablets, USP 24 specifies that in pH 7.2 phosphate buffer, using USP apparatus 2 (paddles) at 50 rpm, at least 80% of the ibuprofen contained in the dosage form is **released** therefrom within 60 minutes after dosing. See USP 24, 2000 Version, 19-20 and 854 (1999).
DETD . . . retained acceptable dissolution characteristics for the desired shelf-life and storage period at elevated temperature and humidity conditions. In particular, the **cellulose**-ether based compositions embodying to the present invention were also advantageously more resistant to microbial growth, which thereby enabled a longer, other dipping dispersions of the present invention may have been higher than that typically found in gelatin-based dipping solutions, the **cellulose**-ether based compositions of the present invention surprisingly required a shorter drying cycle time relative to that for gelatin-containing compositions. Third, . . .

DETD . . .	212.3	566.67	566.67	566.67	566.67	
halofantrin	0	53	53	67	67	
PEG 400	0	7	7	5	5	
Hydroxy-**ethylcellulose**'	0	0	0	0	0	
Total coating solution	233.3	666.67	666.67	666.67	666.67	
Wt % solids in coating solution	94	15%	15	15	15	

'Available from Aqualon, under the tradename, . . .
DETD . . . oil 0 0 0.13
HPMC (1910, 5 mPas) 0 0 32.4 67
PEG 400 5 5 0
Hydroxy-**ethylcellulose**' 24 24 0
Total coating solution 666.67 666.67 722.9
Wt % solids in coating solution 15% 15% 4.5%

'Available from Aqualon, under the . . .
DETD 88.4 kg (9% w/w) of hydroxypropyl **methylcellulose** 2910, 5 mPa·s and 0.347 kg (0.04% w/w) of castor Oil were mixed into 593.8 kg (91% w/w) of purified . . .
DETD Preparation of Tablets Dip **Coated** with HPMC/**Carrageenan** Dipping Solutions
DETD . . . Motor fitted with a 6 cm propeller blade at a speed of 650 rpm for 30 minutes. 7.5 g of **Gellan Gum** ("Kelco gel", Kelco) was then added thereto with constant mixing for 15 min. 2.6 g of colorant

L57 ANSWER 1 OF 79 USPATFULL on STN (Continued)
("Opatint Red DD-3761". . .
DETD
TABLE 0

Hydroxypropyl Starch Based Dipping Solutions

Component	Trade name	Supplier	Amount Used*
Hydroxypropyl Starch	Pure-Cote B790	Grain Processing Corporation	92.5
Gellan Gum	Kelcogel	Kelco	7.5
Colorant	Opatint Red	Colorcon	2.6
Water	N/A	N/A	300

*All values expressed in terms of weight (grams) unless otherwise stated

CLM What is claimed is:
. . . of manufacturing a dosage form comprising a core and coating layer substantially covering the core, wherein the core comprises: a **pharmaceutical** active agent and the coating layer is comprised of: a) a hydroxypropyl starch film former; b) a thickener selected from the group consisting of kappa carrageenan, iota carrageenan, halodentrin, **gellan gum**, agar, and mixtures thereof; and c) a plasticizer, wherein said method comprises dip coating said core in an aqueous dispersion. . . .
CLM What is claimed is:
66. The method of claim 36, wherein the thickener comprises kappa carrageenan, iota carrageenan, **gellan gum**, or a mixture thereof.

CLM What is claimed is:
67. The method of claim 65, wherein the thickener comprises kappa carrageenan, iota carrageenan, **gellan gum**, or a mixture thereof.

CLM What is claimed is:
68. The method of claim 65, wherein the thickener comprises kappa carrageenan, iota carrageenan, **gellan gum**, or a mixture thereof.

IT Drug delivery systems
(capsules; dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT Plasticizers
(dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT Castor oil
IT Polyoxyalkylenes, biological studies
(dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT Coating process
(dip; dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT Drug delivery systems
(tablets, coated; dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT 7631-86-9, Silica, Biological studies
(colloidal; dip coating compns. containing **cellulose** ethers for capsules and tablets)

L57 ANSWER 2 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2008:238144 USPATFULL
TITLE: GRANULE WITH HYDRATED BARRIER MATERIAL
INVENTOR(S): Becker, Nathaniel T., Burlingame, CA, UNITED STATES
Christensen, Robert I., Pinole, CA, UNITED STATES
Gertner, Alfred L., San Bruno, CA, UNITED STATES
Ghani, Mahmood M., Milpitas, CA, UNITED STATES
Dale, Douglas A., Pacifica, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20080268830	A1	20080930
APPLICATION INFO.:	US 2008-113422	A1	20080501 (12)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2003-638217, filed on 30 Jul 2003, ABANDONED Continuation of Ser. No. US 2000-581717, filed on 16 Jun 2000, Pat. No. US 6602841 A 371 of International Ser. No. WO 1998-US27214, filed on 21 Dec 1998

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-68382P	19971220 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	GENENCOR INTERNATIONAL, INC., ATTENTION: LEGAL DEPARTMENT, 925 PAGE MILL ROAD, PALO ALTO, CA, 94304, US	
NUMBER OF CLAIMS:	13	
EXEMPLARY CLAIM:	1	
LINE COUNT:	456	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A granule having high stability and low dust is described. The granule includes a hydrated barrier material having moderate or high water activity. Also described are methods of producing the granules.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM U.S. Pat. No. 6,106,891 describes an improved formation of enzyme granules by including within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-40% w/w based on the dry weight of the whole composition. In addition, the particles . . . distomaceous earth or sodium citrate crystals. The film forming . . . material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.
SUMM . . . and improved stability formulations. Accomplishing all these desired characteristics simultaneously is particularly challenging task since, for example, many delayed **release** or low-dust agents such as fibrous **cellulose** or warp size polymers leave behind insoluble residues.
DETD Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as enzymes.
DETD Suitable coatings include **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidones (PVP), **cellulose** derivatives such as **methylcellulose**, hydroxypropylmethyl **cellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan,

L57 ANSWER 2 OF 79 USPATFULL on STN (Continued)
carrageenan, latex polymers, and ceramic **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.

DETD . . . Preferably, the water coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVA-methylmethacrylate copolymer and PVP-PVA copolymer.

DETD Finally, a polymer coating solution was prepared by dissolving 6.75 kg of Klucel 5% (**hydroxypropyl** cellulose), 7.94 kg titanium dioxide and 1.59 kg Opadal 23-4.97 monomix surfactant in 50.12 kg water and spraying over the . . .

L57 ANSWER 3 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2007:129253 USPATFULL
TITLE: METHOD FOR DIP COATING DOSAGE FORMS
INVENTOR(S): Gallas, Cynthia, Lansdale, PA, UNITED STATES
Gowan, Walter O. JR., Westford, MA, UNITED STATES
Parekh, Kishor R., Horsham, PA, UNITED STATES
Morris, Joseph M., Coatesville, PA, UNITED STATES
Markley, Thomas J., North Wales, PA, UNITED STATES
Wenand, Dennis C., Coopersburg, PA, UNITED STATES
McNally, Gerard P., Berwyn, PA, UNITED STATES
Szymczak, Christopher, Marlton, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20070259098	A1	20071108
APPLICATION INFO.:	US 2007-769028	A1	20070627 (11)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2002-132799, filed on 12 Apr 2002, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-291127P	20010515 (60) <--
	US 2001-325726P	20010920 (60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PHILIP S. JOHNSON, JOHNSON & JOHNSON, ONE JOHNSON &
JOHNSON PLAZA, NEW BRUNSWICK, NJ, 08933-7003, US
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1-30
LINE COUNT: 1431
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Water soluble, gelatin-free dip coatings for **pharmaceutical** solid dosage forms such as tablets comprising HPMC and xanthan gum, carrageenan, and mixtures thereof, or HPMC and castor oil or maltodextrin.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Water soluble, gelatin-free dip coatings for **pharmaceutical** solid dosage forms such as tablets comprising HPMC and xanthan gum, carrageenan, and mixtures thereof, or HPMC and castor oil. . .

SUMM . . . (OTC) drugs. The ability to combine capsule halves having different colors provided manufacturers with a unique means of distinguishing various **pharmaceutical** products. Many patients preferred capsules over tablets, perceiving them as being easier to swallow. This consumer preference prompted **pharmaceutical** manufacturers to market certain products in capsule form even when they were also available in tablet form.

SUMM . . . alternative to capsule products are caplets, which are solid, oblong tablets that are often coated with various polymers such as **cellulose** ethers to improve their aesthetics, stability, and swallowability. Typically, such polymers are applied to the tablets either from solution in. . .

SUMM However, the use of gelatin as a **pharmaceutical** coating material

L57 ANSWER 3 OF 79 USPATFULL on STN (Continued)
presents certain disadvantages and limitations, including the potential for decreased dissolution rate after extended storage due to cross-linking. . . .

SUMM . . . shells via conventional dip molding processing. See also U.S. Pat. No. 4,001,211 (capsules prepared via pin dip coating with thermogelled **methylcellulose** ether compositions). However, due to potential tampering concerns, hard gelatin capsules are no longer a preferred delivery system for consumer (over-the-counter) **pharmaceuticals**, dietary supplements, or other such products. Additionally, the properties of an ideal composition into which steel pins are to be.

SUMM a) hydroxypropylmethyl **cellulose**; and
SUMM a) hydroxypropylmethyl **cellulose**; and
SUMM a) hydroxypropylmethyl **cellulose**; and
DETD . . . parts water required to dissolve 1 part of the non-polymeric, water soluble solute. See Remington, "The Science and Practice of **Pharmacy**," pages 205-207 (2000). "Water soluble," as used herein in connection with polymeric materials, shall mean that the polymer swells in.

DETD Diethicone is a well known **pharmaceutical** material consisting of linear siloxane polymers containing repeating units of the formula: {--(CH.sub.2).sub.2Si(O).sub.n stabilized with trimethylsiloxy end blocking units of. . .

DETD . . . via a dip molding process. One composition comprises, consists. . .

of, and/or consists essentially of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and a thickener, such as a hydrocolloid, e.g., xanthan gum or carrageenan. In another embodiment, the composition comprises, consists of, and/or consists essentially of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; and optionally a plasticizer, such as vegetable oils, e.g., castor oil; and may optionally be substantially free of thickeners such . . . gum. In yet another embodiment, the composition comprises, consists of, and/or consists essentially of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; an extender, such as polyarabinotrans, e.g., nanodentify; and optionally a plasticizer, such as glycols, e.g., polyethylene glycol; and may optionally. . .

DETD . . . use in film forming composition of the present invention. Examples of suitable film formers include, but are not limited to, **polyvinylalcohol** (PVA), hydroxypropyl starch, hydroxyethyl starch, pullulan, methylethyl starch, carboxymethyl starch, **methylcellulose**, **hydroxypropylcellulose** (HPC), **hydroxyethylmethylcellulose** (HEMC), **hydroxypropylmethylcellulose** (HPMC), **hydroxybutylmethylcellulose** (HBMC), **hydroxyethylethylcellulose** (HEEC),
hydroxyethylhydroxypropylmethyl **cellulose** (HEMPMC), pre-gelatinized starches, and polymers and derivatives and mixtures thereof.

DETD One suitable **hydroxypropylmethylcellulose** compound is "HPMC 2910", which is a **cellulose** ether having a degree of substitution of about 1.9 and a hydroxypropyl molar substitution of 0.23, and containing, based upon. . .

DETD Any plasticizer known in the pharmaceutical art is suitable for use in the present invention, and may include, but not be limited to polyethylene glycol; glycerin. . . glycol; mono acetate of glycerol;
diacetate of glycerol; triacetate of glycerol; natural gums and
natures

L57 ANSWER 3 OF 79 USPATFULL on STN (Continued)
thereof. In solutions containing a **cellulose** ether film former, an optional plasticizer may be present in an amount, based upon the total weight of the solution, . . .

DETD In embodiments wherein a **cellulose** ether film former is used in the composition, the film forming composition for dip coating substrates may
be substantially free. . .

DETD . . . than about 100 percent, e.g. from about 95 percent to about 99.5 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; and from about 0.5 percent to about 5 percent of a thickener such as a hydrocolloid, e.g., xanthan gum.

DETD . . . to about 100 percent e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**.

DETD . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and substantially free of hydrocolloids, i.e., e.g. contains less than about 1%, or less than about 0.01% of hydrocolloids.

DETD . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; and from about 0.1 percent to about 1.0 percent, e.g. from about 0.25 percent to about 0.5 percent of a.

DETD . . . to about 90 percent, or from about 80 percent to about 90 percent of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; from about 1 percent to about 80 percent, e.g. from about 5 percent to about 50 percent or from about.

DETD . . . percent to about 15 percent or from about 10 percent to about 14 percent, of a film former such as **hydroxypropylmethylcellulose** and from about 0.05 percent to about 0.2 percent, e.g. from about 0.08 percent to about 0.16 percent or from.

DETD . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**

DETD . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and is substantially free of hydrocolloids, i.e., e.g. contains less than about 1%, or less than about 0.01% of hydrocolloids.

DETD . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.001 percent to about 0.1 percent, e.g. from about 0.01 percent to about 0.09 percent of a. .

DETD . . . to about 19 percent or from about 16 percent to about 19 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, from about 0.1 percent to about 17 percent, e.g. from about 1 percent to about 11 percent or from about.

DETD . . . opacifying agents such as titanium dioxide, and/or from about 0 percent to about 14 percent colorants. See Remington's Practice of **Pharmacy**, Martin & Cook. 17.sup.th ed., pp. 1625-70, which is herein

L57 ANSWER 3 OF 79 USPATFULL on STN (Continued)
DETD incorporated by reference.
DETD Any coloring agent suitable for use in **pharmaceutical** applications may be used in the present invention and may include, but not be limited to azo dyes, quinophthalone dyes
DETD In one embodiment, the **pharmaceutical** dosage form is comprised of a) a core containing an active ingredient; b) an optional first coating layer comprised of . . .
DETD . . . and 6,274,162, which are all incorporated by reference herein.
Additional suitable enhancing includes those as more of the following ingredients: **cellulose** ethers such as **hydroxypropylmethylcellulose, hydroxypropylcellulose,** and **hydroxyethylcellulose;** polysaccharides such as xanthan gum, starch, and maltodextrin; polyhydric alcohols including for example, glycerin, polyethylene glycol, propylene glycol, dibutyl sebecate, triethyl.
DETD . . . from about 2 percent to about 8 percent, e.g. from about 6 percent to about 8 percent of a water-soluble **cellulose** ether and from about 0.1 percent to about 1 percent, castor oil, as disclosed in detail in U.S. Pat. No. . . .
DETD In one embodiment, the film former is a **cellulose** ether such as HPMC, and the thickener is a hydrocolloid such as xanthan gun and the weight gain achieves; i.e. . . .
DETD . . . any material that can be carried by or entrained in the system. For example, the active agent can be a **pharmaceutical,** nutraceutical, vitamin, dietary supplement, nutrient, herb, foodstuff, dyestuff, nutritional, mineral, supplement, or flavoring agent or the like and combinations thereof.
DETD . . . methenamine mandelate; menthol; meperidine hydrochloride; metaproterenol sulfate; methscopolamine and its nitrates; methserqide and its malate; methyl nicotinate; methyl salicylate methyl **cellulose;** methsuximide; metoclopramide and its halides/hydrates; metronidazole; metoprolol tartrate; miconazole nitrate; mineral oil; minoxidil; morphine; naproxen and its alkali metal sodium. . . . of active drugs or a magnesium trisilicate base and on a magnesium aluminum
. . . silicate base, and mixtures thereof. Mixtures and **pharmaceutically** acceptable salts of these and other actives can be used.
DETD In one embodiment, the dosage forms coated with the dip coatings of the present invention provided for immediate **release** of the active ingredient, i.e. the dissolution of the dosage form conformed to USP specifications for immediate **release** tablets containing the particular active ingredient employed. For example, for acetaminophen tablets, USP 24 specifies that in pH 5.8 phosphate . . . using USP apparatus 2 (paddles) at 50 rpm, at least 80% of the acetaminophen contained in the dosage form is **released** therefrom within 30 minutes after dosing, and for ibuprofen tablets, USP 24 specifies that in pH 7.2 phosphate buffer, using USP apparatus 2 (paddles) at 50 rpm, at least 80% of the ibuprofen contained in the dosage form is **released** therefrom within 60 minutes after dosing. See USP 24, 2000 Version, 19-20 and 856 (1999).

L57 ANSWER 3 OF 79 USPATFULL on STN (Continued)
. . . (a) dipping the core into a dipping solution, wherein the dipping solution comprises the hydroxypropylmethyl **cellulose** and the thickener; and (b) drying the dipped core of step (a).
CLM What is claimed is:
. . . upon the total dry weight of the outer coating, (a) from about 40 percent to about 99.5 percent of hydroxypropylmethyl **cellulose;** and (b) from about 0.5 percent to about 5 percent of the thickener.
CLM What is claimed is:
56. The method of claim 55, wherein the subcoating comprises materials selected from the group consisting of **cellulose** ethers, plasticizers, polyoxahydrates, pigments, opacifiers, and mixtures thereof.
CLM What is claimed is:
57. The method of claim 55 wherein the subcoating comprises materials selected from the group consisting of **hydroxypropylmethylcellulose,** castor oil, polyethylene glycol, polysorbate 80, maltodextrin, and mixtures thereof.
CLM What is claimed is:
. . . total dry weight of the coated dosage form, (a) from about 2 percent to about 8 percent of a water-soluble **cellulose** ether selected from the group consisting of **hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxyethylcellulose,** and mixtures thereof. (b) from about 0.1 percent to about 1 percent castor oil.
CLM What is claimed is:
. . . based upon the total dry weight of the coated dosage form, (a) from about 4 percent to about 6percent **hydroxypropylmethylcellulose;** and (b) from about 0.1 percent to about 1 percent castor oil.
CLM What is claimed is:
(a) . . . comprised of, based upon the total dry weight of the subcoating, from about 20 percent to about 50 percent **hydroxypropylmethylcellulose;** (b) from about 45 percent to about 75 percent maltodextrin; and (c) from about 1 percent to about 10 percent.
CLM What is claimed is:
(a) . . . comprised of, based upon the total dry weight of the subcoating, from about 25 percent to about 40 percent **hydroxyethylcellulose;** (b) from about 50 percent to about 70 percent maltodextrin; (c) from about 5 percent to about 10 percent PEG. . . .
CLM What is claimed is:
. . . solution comprises, based upon the total weight of the solution, (a) from about 10 percent to about 14 percent of **hydroxypropylmethylcellulose;** and (b) from about 0.1 percent to about 0.14 percent of xanthan gun.
CLM What is claimed is:
67. The method of claim 61, wherein the coated dosage form meets USP dissolution requirements for immediate **release** forms of the **pharmaceutical** active ingredient.

L57 ANSWER 3 OF 79 USPATFULL on STN (Continued)
DETD . . . retained acceptable dissolution characteristics for the desired shelf-life and storage period at elevated temperature and humidity conditions. In particular, the **cellulose**-ether based compositions according to the present invention were also advantageously . . . more resistant to microbial growth, which thereby enabled a longer. . . . other dipping dispersions of the present invention may have been higher than that typically found in gelatin-based dipping solutions, the **cellulose**-ether based compositions of the present invention surprisingly required a shorter drying cycle time relative to that for gelatin-containing compositions. Third, . . .

DETD . . .	212.3	566.67	566.67	566.67	566.67
Maltodextrin	0	53	53	67	67
PEG 400	0	7	7	5	5
Hydroxy-	0	0	0	0	0
ethylcellulose*					
Total coating solution	233.3	666.67	666.67	666.67	666.67
Wt % solids in coating solution	9%	15%	15	15	15

*Available from Aqualon, under the tradename, . . .

DETD . . . oil	0	0	0	0.13
HPMC (1910, 5 mPas)	0	0	32.4	
PEG 400	5	5	0	
Hydroxy-	24	24	0	
ethylcellulose*				
Total coating solution	666.67	666.67	722.9	
Wt % solids in coating solution	15%	15%	4.5%	

*Available from Aqualon, under the. . .
DETD 88.4 kg (9% w/w) of hydroxypropyl **methylcellulose** 2910, 5 mPa and 0.347 kg (0.04% w/w) of castor Oil were mixed into 593.8 kg (91% w/w) of purified. . . .
DETD Preparation of Tablets Dip **Coated** with HPMC/**Carrageenan** Dipping Solutions
CLM What is claimed is:
31. A water soluble composition for dip-coating a substrate comprised of: a) hydroxypropylmethyl **cellulose;** and b) castor oil, wherein the composition possesses a surface gloss of at least 150 when applied via dip coating. . . .
CLM What is claimed is:
. . . having a core and an outer coating on the surface of the coated dosage form, wherein the core comprises a **pharmaceutical** active ingredient and the outer coating couples hydroxypropylmethyl **cellulose** and a thickener selected from the group consisting of xanthan gum, carrageenan, and mixtures thereof, the method comprising:

L57 ANSWER 3 OF 79 USPATFULL on STN (Continued)
IT Drug delivery systems
(capsules; dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT Plasticizers
(dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT Castor oil
IT Polyoxyalkylenes, biological studies
(dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT Coating process
(dip; dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT Drug delivery systems
(tablets, coated; dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT 7631-86-9, Silica, biological studies
(occlusion; dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT 9050-81-5, Dimethicone **9000-07-1,** Carrageenan 9004-62-0, Hydroxyethyl **cellulose** 9004-64-2, Hydroxypropyl **cellulose** 9004-65-3, Hydroxypropyl methyl **cellulose** 9049-76-7, Purity Gum 59 9050-36-6, Maltodextrin 11114-20-8, κ-Carrageenan 11138-66-2, Xanthan gun 25322-68-3, Polyethylene glycol
(dip **coating** compns. containing **cellulose** ethers for capsules and tablets)
IT **9000-07-1,** Carrageenan
(dip **coating** compns. containing **cellulose** ethers for capsules and tablets)

L57 ANSWER 4 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2006:101146 USPATFULL
TITLE: Film forming compositions comprising modified starches and iota-carrageenan and methods for manufacturing
soft
capsules using same
INVENTOR(S): Tanner, Keith Edward, Safety Harbor, FL, UNITED STATES
Draper, Peter Robert, LaBelle, CHMADA
Getz, John J., Delray Beach, FL, UNITED STATES
Burnett, Stephen W., Clearwater, FL, UNITED STATES
Youngblood, Elizabeth, Wairiko, FL, UNITED STATES
PATENT ASSIGNEE(S): R.P. Scherer Technologies, Inc., Las Vegas, NV, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20079	E1	20060425
	US 6340473		20020122 (Original)
APPLICATION INFO.:	US 2004-764382		20040122 (10)
	US 2000-608853		20000630 (Original)<--

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-142704P	19990701 (60) <--
DOCUMENT TYPE:	Reissue	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Page, Michael G.	
LEGAL REPRESENTATIVE:	Dippert, William H., Korycki, Andrew G., Nickey, Donald	
NUMBER OF CLAIMS:	0.	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	1139	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed herein are compositions comprising a modified starch and a carrageenan, especially iota-carrageenan, where the compositions are suitable for use in manufacturing soft capsules.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM01 Encapsulation within a soft capsule of a solution or dispersion of a nutritional or **pharmaceutical** agent in a liquid carrier offers many advantages over other dosage forms such as compressed, coated or uncoated solid tablets. . . .

SUM01 Soft encapsulation of drugs further provides the potential to improve the bioavailability of **pharmaceutical** agents. Active ingredients are rapidly **released** in liquid form as soon as the gelatin shell ruptures. Complete disintegration of the capsule is not necessary for the. . .

SUM01 . . . and cut. Rotary die manufacture of soft gelatin capsules is disclosed in detail in The Theory and Practice of Industrial **Pharmacy** (Lachman, Lieberman and Kanig, Editors), 3.sup.rd Edition, published by Lea & Febiger. A good description of gelatin encapsulation techniques

L57 ANSWER 4 OF 79 USPATFULL on STN (Continued)
the shell. . .

SUM01 . . . allow the film to be reversibly stretched during the capsule filling step. These compositions, as wet films, preferably comprise water, 6-**12** weight % iota-**carrageenan**, **12**-30 weight % modified starch, 3-30 weight % plasticizers, 0.5-2 weight % buffers and optionally 0-0.2 weight % preservatives.

SUM01 There is further disclosed soft, edible, soft capsule which comprises:

a) a soft, dry shell which comprises:
(i) about **12**-**24** weight % iota-**carrageenan**;
(ii) about 30-60 weight % modified starch;
(iii) about 10-60 weight % plasticizer;
(iv) about 1-4 weight % sodium or dibasic buffer system. . .

SUM01 In iota-**carrageenan**, the **1**,3- and 3,4-linked units are respectively D-galactose-4-sulfate and 3,6-anhydro-D-galactose-2-sulfate. However, some of the 3,6-anhydro-D-galactose-2-sulfate rings may be replaced by D-galactose-4-sulfate, which.

SUM01
TABLE II

Typical Analytical Parameters and Values for Iota-carrageenan

Parameter	Typical Values (Na-Iota)	Typical Values (Ca-Iota)
Gel strength	0-100 g/cm.sup.2 (1.5% **carrageenan**)	0
pH	7-10 (i.e. 1.5% gel)	7-10
Viscosity	10-30 cP (1.5% at 75° C.)	10-30
Chloride	0-3% (as KCl)	0-3%
Calcium	2-6%	0-0.5%

. . .

SUM01 . . . colorants and diluents/grants. The inventive compositions are typically in the molten state when these components are added. Use of conventional **pharmaceutical** or food grade ingredients is acceptable.

SUM01 . . . preferred amounts of iota-carrageenan range from about 7-12% by

weight of the wet composition. Particularly preferred compositions contain from about 9-**11** weight % of iota-**carrageenan**, based on the weight of the wet composition. Even more preferred compositions contain about **10** weight % of iota-**carrageenan** by weight of the wet composition.

SUM01 . . . in accordance with conventional techniques as set forth in Ebert, E. W., "Soft elastic gelatin capsules: a unique dosage form", **Pharmaceutical** Tech., October 1977; Stanley, J. P., "Soft Gelatin Capsules", in The Theory and Practice of Industrial **Pharmacy**, 359-84 (Lea and Febiger ed. 1970); U.S. Pat. Nos. 1,970,396; 2,288,327; and 2,718,733.

SUM01 . . . and will recognize suitable fill materials. These fill materials may contain sweetics, foods including vitamins, liquids, semi-solids, suspensions, flavorings and **pharmaceuticals**. After filling, the capsules are typically dried according to conventional techniques, e.g., tray drying, using a drum dryer or other. .

DETD

Formulation 7
Native Potato Starch
Wet Film

L57 ANSWER 4 OF 79 USPATFULL on STN (Continued)
can. . .

SUM01 . . . capsule having outstanding physical properties. Further, there is no disclosure or suggestion that a weight ratio of modified starch to

iota-**carrageenan** of at least 1.5:1 is required to produce a film that can be used in a rotary die encapsulation machine to make soft capsules.

SUM01 PCT Application WO 00/10538 to Banner **Pharmacaps** discloses a gelatin free capsule comprising:

a) 5-50% by weight of a water dispersible or water-soluble plasticizer;
b) 0.5-**121** by weight kappa **carrageenan**;
c) 0-60% by weight dextrins; and
d) 1-95% by weight water wherein the kappa carrageenan comprises at least 50% by weight of. . .

SUM01 . . . a heat sealable, edible film comprising a film layer consisting

essentially of: 1) a water soluble polysaccharide composed chiefly of **carrageenan**, **2**) a polyhydric alcohol; and 3) water. The film of this patent has a water content of not greater than 15%. . . .

SUM01 . . . a gelatin and at least 1% by weight of an agent selected from the group consisting of starches, starch derivatives, **cellulose**, **cellulose** derivatives, milk powder, non-hygroscopic mono-, di- and oligo saccharides, magnesium trisilicate and silicon dioxide. These agents are described as being. . .

SUM01 . . . instead, require at least two (2) agents: 1) a modified starch having a hydration temperature below about 90° C. and **2**) iota-**carrageenan**.

SUM01
TABLE I

Prototypic Formula
Component Weight % of Wet Film Weight % of Dry Film

Iota-**carrageenan**	6-**12**	**12**-**24**
Modified starch	12-30	30-60
Plasticizer	5-30	10-60
Buffer	0.5-2	1-4
Preservative	0-0.2	0-0.4

SUM01 . . . starch to the iota-carrageenan is crucial to forming a satisfactory film. The weight ratio of the modified starch to the iota-**carrageenan** is at least **1**.5:1, with a preferred range being 1.5:1 to 4:1. Another feature useful in characterizing the inventive film is fusion pressure. The. . .

SUM01 . . . least about 207 kPa (30 psi). There is further disclosed a composition wherein the weight ratio of modified starch to iota-**carrageenan** ranges from **1**.5:1 to 4:1, more preferably from 2:1 to 3:1. Further, the invention relates to a film forming composition that is capable. . .

SUM01 . . . wherein said starch has a hydration temperature below about 90° C. and wherein the weight ratio of modified starch in iota-**carrageenan** ranges from **1**.5:1 to 4.0:1. The invention also relates to a soft capsule comprising a shell and a fill material wherein

L57 ANSWER 4 OF 79 USPATFULL on STN (Continued)
Ingredient Percent by weight

Potato Starch Supra Baster (Roquette)	**15**.8
Iota-**carrageenan**	8.0
Glycerin USP	15.0
Sodium phosphate di basic	1.0
Preservative	0.20
Water USP	60.0

DETD

Formulation 9
Kappa only - no Iota
Ingredient Percent by weight

PURE-COTE ®	**20**.0
Kappa-**carrageenan**	6.0
Xanthan gum	2.0
Glycerin USP	20.0
Sodium phosphate di basic	1.0
Preservative	0.20
Water USP	50.8

DETD . . . a weak character compared to Formulations 1, 3 and 4. This could be the result of the modified starch to iota-**carrageenan** ratio of 1.5:1, whereas Formulations 3 and 4 had starch to carrageenan weight ratios in excess of 2.0:1. Formulation 5 yielded a good film, but

the sealing characteristics were poorer than Formulations 3 and 4; this could be due to the high, 2.5:1, starch to **carrageenan** ratio. Formulation 7, the only unmodified starch that was found to work with iota-carrageenan was found to cast an acceptable. . . .

DETD A standard rotary die machine (see The Theory and Practice of Industrial **Pharmacy**, Lachman, Lieberman and Kanig, Editors, 3.sup.rd Edition, published by Lea & Febiger, was used to attempt the manufacture of filled. . . .

DETD . . . for 2 months at 40° C./75% Relative Humidity ("RH"), which is a standard condition used to accelerate stability evaluation of

pharmaceutical dosage forms. A nanmalian gelatin based softgel filled with mineral oil wa also evaluated using the save conditions as a. . .

DETD . . . only carrageenan composition was made essentially according to the description set forth in published International Application WO 97/07347, except that **17**% **carrageenan** is used instead of 9% as described in the International Application. Table III set s forth the melting point of each. . .

DETD
TABLE III

	CONTROL Gelatin	INVENTION Starch/Carrageenan	CONTROL **Carrageenans**
Formulation	70-85% gelatin; 10-30% plasticizer,	**15**-20% starch; 10% iota-**carrageenan**	17% iota-**carrageenan**

L57 ANSWER 4 OF 79 USPATFULL on STN (Continued)
water, 0.4.
Typical Melt 50-55° C. 80-85° C. 95-98°
Temperature
Operational 60-65° C. About 98-100° C.
Casting
Fusion 60-62° C. 53-75° C. . .
DS7D . . . #18 #19 #20 #21 #22 #23 #24 #25 #26
#27

.sup.1Kappa 5.65 5.65 10.0 10.0 5.0 2.5 1.0 10.0 0.0
10.0 **10.0** **10.0**
carrageenan
.sup.1Lambda 5.65
carrageenan
.sup.1Iota 5.65 5.0 7.5 9.0
carrageenan
.sup.2Pure Cote .TM. 15.0 22.0 27.3 27.3 27.3 13.55
20.0 20.0 20.0 23.0 27.3 20.0 15.0

B76G
Water. . . 0.2
Na.sub.2EPO.sub.4 3.0 3.0 3.0 3.0 3.0 3.0 3.0
3.0 3.0 1.0 1.0 1.0
Locust Bean 0.25
0.5 1.0
Gum
Xanthan Gum
0.5
.sup.3XPO-AFK 10.0 **10.0**
Kappa
carrageenan
.sup.3XPO-CM1 5.5 10.0 10.0
Iota/Kappa
blend

.sup.1Supplied by FMC Corporation of Princeton, New Jersey
.sup.2Hydroxypropylated maize starch
.sup.3Supplied by SSW Biosystems
DS7D
TABLE V

Component #28 #29 #30 #31

.sup.1Lambda **carrageenan** **10.0**
.sup.1Iota-carrageenan 10.0
LC-5 standardized
with sucrose
Pure Cote .TM. B79G 15.0 27.3 27.3
.sup.2TPS-1 non-standardized Iota 10.0
.sup.3XPO-KG1 Iota 10.0
Water 56.3 46.5 46.5 68.8
Glycerin 17.5. . .
DS7D
TABLE VII

L57 ANSWER 5 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2001:37026 USPATFULL
TITLE: Matrix granule
INVENTOR(S): Becker, Nathaniel T., Hillsborough, CA, UNITED STATES
Green, Thomas S., Montara, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20010031701	A1	20050210
	US 7500779	B2	20071127
APPLICATION INFO.:	US 2004-939076	A1	20040913 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2002-180785, filed on 25 Jun 2002, GRANTED, Pat. No. US 6790643 Continuation of Ser. No. US 1999-428153, filed on 27 Oct 1999, GRANTED,		
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	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-105874P	19981027 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	JEFFERY D. FRASSER, GRUNECOR INTERNATIONAL, INC., 925 PAGE MILL ROAD, PALO ALTO, CA, 94304-1013	
NUMBER OF CLAIMS:	20	
EXEMPLARY CLAIM:	1	
LINE COUNT:	529	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Granules that include a protein core are described. The protein core includes a protein matrix which includes a protein mixed together with a
starch. The protein matrix can be layered over a seed particle or the protein core can be homogeneous. The protein can be an enzyme or a therapeutic protein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM0 [0002] Proteins such as **pharmaceutically** important proteins like hormones and industrially important proteins like enzymes are becoming more widely used. Enzymes are used in several. . . .
SUM0 . . . U.S. Pat. No. 5,679,392 describes an improved formulation of enzyme granules by including within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-60% w/w based on the dry weight of the whole composition. In addition, this patent. . . .
SUM0 . . . diatomaceous earth or sodium citrate crystals. The film forming
material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.
SUM0 perborate or sodium percarbonate. Accomplishing all these desired characteristics simultaneously is a particularly challenging task since, for example, many delayed **release** or low-dust agents such as fibrous **cellulose** or kaolin leave behind insoluble residues.
SUM0 between the seed particle and the matrix or the matrix and the barrier layer, for example, a coating such as **polyvinyl** alcohol (PVA).
SUM0 [0030] Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as enzymes.

L57 ANSWER 6 OF 79 USPATFULL on STN (Continued)
Weight % In Wet Composition
Component
#34 #35
Iota-**carrageenan** (Viscarin SD389) **10.25** 10.25
Hydroxypropylated tapioca starch 25.75 0
Glycerin 21.40 21.40
Potassium phosphate 41.60 41.60
Water 1.0 1.0
Hydroxypropylated maize starch
DS7D . . . possess certain specific properties. While mammalian gelatin has received the gelling agent of choice, there are numerous shortcomings that the **pharmaceutical** industry would like to overcome with new, non-gelatin soft capsules. . . .
DS7D . . . a discovery regarding the synergistic activity between a specific form of carrageenan and certain modified starches, will provide
to the **pharmaceutical** industry an alternative to mammalian gelatin. It was through diligent experimentation and scientific observation that the
inventive compositions were realized.
CLM What is claimed is:
1. An edible, soft capsule which comprises a soft, dry shell which comprises: ((v)) (a) about **12-24** weight % iota-**carrageenan**; ((v1)) (b) about 30-60 weight % modified starch; ((v1i)) (c) about 10-60 weight % plasticizer; and. . . .
CLM What is claimed is:
7. An edible, soft capsule which comprises a soft, dry **shell** which comprises: (a) iota-**carrageenan**; (b) modified starch; and (c) plasticizer, wherein the weight ratio of iota-carrageenan to modified starch is at least 1.5:1 and. . . .
CLM What is claimed is:
4. An edible, soft capsule which comprises: (a) a soft dry **shell** comprising: (i) iota-**carrageenan**; (ii) modified starch; and (iii) plasticizer, wherein the weight ratio of iota-carrageenan to modified starch is at least 1.5:1, and. . . .
CLM What is claimed is:
6. An edible, soft capsule, which comprises a soft, dry shell which comprises: (a) about **12-24** weight % iota-**carrageenan**; (b) about 30-60 weight % modified starch; (c) about 10-60 weight % plasticizer; and (d) about 1-4 weight % buffer, . . .

L57 ANSWER 7 OF 79 USPATFULL on STN (Continued)
SUM0 . . . more synthetic polymers or other excipients as known to those skilled in the art. Suitable synthetic polymers include polyethylene oxide, **polyvinyl** alcohol, **polyvinyl** pyrrolidone, polyethylene glycol and polyethylene oxide/polypropylene oxide.
SUM0 [0036] Suitable coatings include water soluble or water dispersible film-forming polymers such as **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, gum arabic, xanthan, **carrageenan**, chitosan, latex polymers, and enteric **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.
SUM0 Preferably, the outer coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVO-methylmethacrylate copolymer and PVP-PVA copolymer.
DS7D . . . cosmetically coated with 92.6 kg of an aqueous solution containing 7.1 kg (6.2% w/w) titanium dioxide, 2.9 kg (2.5% w/w) **methylcellulose**, 2.9 kg (2.5%) Purecote B790, 1.2 kg (1.1% w/w) Neodol 23/6.5, and 2.0 kg (1.67% w/w) of polyethylene glycol at. . . .
CLM What is claimed is:
6. The granule of claim 3, wherein the coating is selected from the group consisting of **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan and carrageenan.

L57 ANSWER 6 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2005:16441 USPATFULL
TITLE: Functional powders for oral delivery
INVENTOR(S): Tobyn, Michael John, Wiltshire, UNITED KINGDOM
Staniforth, John Nicholas, Bath, UNITED KINGDOM
Simpson, David Bradley Brook, Bath, UNITED KINGDOM
PATENT ASSIGNEE(S): Ventura Limited, Chippenham, UNITED KINGDOM, SN14 6FH (non-U.S. corporation)

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	WO 2002-IB4101		20020905

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PRIORITY INFORMATION:	US 2001-317522P	20010905 (60)
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FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	DAVIDSON, DAVIDSON & KAPPEL, LLC, 485 SEVENTH AVENUE, 14TH FLOOR, NEW YORK, NY, 10018	
NUMBER OF CLAIMS:	191	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	13 Drawing Page(s)	
LINE COUNT:	5183	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB In certain embodiments the invention is directed to a drug formulation for gastrointestinal deposition comprising a non-compressed free flowing plurality of particles comprising a core comprising a drug and a **pharmaceutically** acceptable excipient, said cores overcoated with a functional coating, said drug particles having a mean diameter of greater than 10 μm to about 1 mm.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . formulation for gastrointestinal deposition comprising a non-compressed free flowing plurality of particles comprising a core comprising a drug and a **pharmaceutically** acceptable excipient, said cores overcoated with a functional coating, said drug particles having a mean diameter of greater than 10 μm to about 1 mm.

SUMM . . . improve compressibility or to aid in disintegration after administration. However, these added excipients have been shown to adversely influence the **release**, stability and bioavailability of the active ingredient. The added excipients are a particular problem with drugs which require a high . . .

SUMM . . . many therapeutic agents are not sufficiently stable in solution/suspension form. Indeed, most suspension type formulations are typically reconstituted by the **pharmacist** and so have a limited shelf life even under refrigerated conditions. Another problem with liquid formulations which is not an . . .

SUMM . . . an object of certain embodiments of the invention to provide a coated multiparticulate formulation which provides a controlled or

L57 ANSWER 6 OF 79 USPATFULL on STN (Continued)
gastrointestinal deposition. For example, the excipient can provide a controlled **release** of the drug upon gastrointestinal deposition to provide a therapeutic effect for at least 12 hours after oral administration. In other embodiments, the excipient can provide a controlled **release** of the drug upon gastrointestinal deposition to provide a therapeutic effect for at least 24 hours after oral administration.

DETD [0122] In other embodiments, the excipient can provide a delayed **release** (e.g., via an enteric coating) of the drug upon gastrointestinal deposition, such as delaying **release** of the drug to the distal intestinal absorption site, substantially to the gastric mucosa.

DETD [0127] For example, the functional coating can provide a controlled or delayed **release** of the drug upon gastrointestinal deposition; the functional coating can provide taste masking; the functional coating can comprise a salivary stimulant. . . . The same is true in the core, for example, when the core is coated with an excipient that provides controlled **release** and the drug is underlying the drug . . .

DETD [0139] Controlled **release** materials useful in the present invention are preferably hydrophobic materials. The hydrophobic materials can be selected from the group consisting of an acrylic polymer, a **cellulosic** material, shellac, zein and mixtures thereof.

DETD [0137] When the controlled **release** material is a **cellulosic** material, the **cellulosic** material is, e.g., selected from the group consisting of **cellulose** esters, **cellulose** diesters, **cellulose** triesters, **cellulose** ethers, **cellulose** ester-ethers, **cellulose** acylats, **cellulose** diacylate, **cellulose** triacylate, **cellulose** acetate, **cellulose** diacetate, **cellulose** triacetate, **cellulose** acetate propionate, **cellulose** acetate butyrate and mixtures thereof.

DETD [0138] Particularly preferred controlled **release** materials are **ethylcellulose**, polymethacrylates, e.g. Eudragit RL and RS, glyceryl behenate, **methylcellulose** and sodium **carboxymethylcellulose**.

DETD [0139] In other embodiments of the invention, the controlled **release** material comprises a lacquer material. The lacquer material can be selected, e.g., from the group consisting of corn oil, sesame oil, . . .

DETD [0140] The use of lacquer agents may not **release** the drug of the multiparticulates. Therefore it may be necessary to include a channeling agent in an amount sufficient to provide the desired **release** of the drug, e.g., over 12 or 24 hours. Suitable channeling agents include **polyvinylpyrrolidone**, polyethyleneglycols, dextrose, sucrose, mannitol, xylitol and lactose. Antioxidants may also be added in order to reduce polymerization which leads to . . .

DETD [0141] The use of lacquer agents is beneficial as it reduces the amount of excipient needed to provide a controlled **release** of the drug from the particles of the present invention. In certain embodiments, less than about 15 lacquer is needed . . .

DETD [0142] The lacquer material can be granulated with the drug in order to provide controlled **release** matrices or can coat the drug particulates. The use of lacquer materials is disclosed as providing controlled **release** in multiparticulate dosage forms. However, it also contemplated by the present invention that the use of lacquer agents with optional . . . channeling agents and dispersing agents can also be used in solid dosage forms such as tablets. For example, an immediate **release** tablet core can be coated with sustained **release** coating

L57 ANSWER 6 OF 79 USPATFULL on STN (Continued)
delayed **release** of the active agent contained therein.

SUMM . . . formulation for gastrointestinal deposition comprising a non-compressed free flowing plurality of particles comprising a core comprising a drug and a **pharmaceutically** acceptable excipient, said core overcoated with a functional coating.

SUMM . . . provides a drug formulation for gastrointestinal deposition comprising a non-compressed free flowing plurality of particles comprising a drug and a **pharmaceutically** acceptable excipient, said particles having a mean diameter of greater than 10 μm to about 1 mm. [0046] In certain embodiments of the invention, the multiparticulates comprise a **pharmaceutically** acceptable excipient. The excipient preferably does not comprise more than about 15% by weight of the formulation; more preferably not . . .

SUMM . . . exert a local effect. Pulmonary deposition means the intended deposit of drug into the lungs in order to provide a **pharmaceutical** effect, regardless that the unit dose may enter the oral cavity prior to pulmonary deposition.

SUMM [0062] The term "functional coat" means a coating on a drug particle which provides a controlled **release** of the drug (e.g., a sustained **release**), a delayed **release** of the drug (e.g., via an enteric coating), taste masking, delivery stimulation, a moisture barrier, texture modification, elimination of surface . . .

DETD . . . deposition of the invention provides a non-compressed free flowing plurality of particles comprising a core comprising a drug and a **pharmaceutically** acceptable excipient, with the core overcoated with a functional coating.

DETD . . . for gastrointestinal deposition comprising preparing a non-compressed free flowing plurality of particles comprising a core comprising a drug and a **pharmaceutically** acceptable excipient as disclosed herein and air jet sieving the particles to separate the cores from fine particles; and thereafter . . .

DETD . . . capable of metering a unit dose of the composition for oral delivery. These compositions can be coated as by for sustained **release** or tasteasking) before air jet sieving, after air jet sieving or not coated at all. The core embodiments are . . .

DETD . . . characteristics are met. In preferred embodiments, the core is formed by mixing drug with excipient, e.g. microcrystalline **cellulose**, **polyvinylpyrrolidone** to form a granulate which is then sieved and coated with further excipient as described. **Ethylcellulose** cores can then be coated with a functional coating (e.g. microcrystalline **cellulose**, . . .

DETD . . . is necessary to increase the amount of functional coat. An increase in functional coat can result in a delayed drug **release** with variable batch to batch dissolution rates. In certain embodiments, the final products prepared with a melt granulation step has minimal batch to batch variability and an acceptable quality profile (e.g., n=3, without an unwanted delay. As with wet granulation embodiments, the application of the functional coat of the invention . . .

DETD [0111] In certain embodiments, the excipient of the core provides a controlled **release** (e.g., a sustained **release**) of the drug upon

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comprising a lacquer agent as disclosed above with an optional channeling agent and dispersing agent. In these embodiments as . . .

DETD [0142] Preferably, the delayed **release** material useful in the present invention are enteric polymers. The enteric polymers can be selected from, e.g., the group consisting of methacrylic acid copolymers, **cellulose** acetate phthalate, hydroxypropyl **methylcellulose** phthalate, hydroxypropyl **methylcellulose** acetate succinate, hydroxypropyl **methylcellulose** phthalate and shellac. Surestick.TM. is an example of a **polyvinyl** acetate phthalate taste masking. Acryl-eze.TM. is an example of a methacrylic acid copolymer based enteric coating.

DETD . . . The dipeptide based sweetener is preferably L-aspartyl L-phenylalanine methyl ester. Examples of preferred taste masking agents are glyceryl behenate, glyceryl palmitostearate, **ethylcellulose** and polymethacrylates such as Eudragit E, EPO and RL.

DETD . . . acrylic acid polymers and copolymers (polyacrylamides, polyacrylestersters, polyalkylcyanoacrylates, polymethacrylates), agar-agar, agaroses, albumin, alginic acid and alginates, carboxyvinyl polymers, **cellulose** derivatives such as cellulose acetate, polyamides (nylon 6-10, polyladipyl-L-lysines, polytrephthalamides and poly-(tetraphthaloyl-L-lysines)), poly-α-caprolactam, polydimethylsiloxane, polyesters, poly(ethylene-vinyl acetate), polyglycolic acid, polylactic acid and its copolymers, polylactanic acid, polylysine, polystyrene, shellac, xanthan gum, anionic polymers of methacrylic acid and methacrylic acid esters, **hydroxyalkylcellulose** and mixtures thereof. In certain embodiments, the enteric barrier material is a **hydroxyalkylcellulose** such as **hydroxypropylmethylcellulose**, a **cellulosic** material such as microcrystalline **cellulose**, carrageenan or mixtures thereof. Particularly preferred enteric barrier materials are microcrystalline **cellulose**/carrageenan-based coating systems such as Lattice(tm), **ethylcellulose** such as Aquacoat ECD (formulated as a 30:80 mixture with **hydroxypropylmethylcellulose**, requiring a alcohol based systems such as Opadry AMB. The above disclosed lacquer agents can also be used as moisture barriers. . . .

DETD . . . acrylic acid polymers and copolymers (polyacrylamides, polyacrylestersters, polyalkylcyanoacrylates, polymethacrylates), agar-agar, agaroses, albumin, alginic acid and alginates, carboxyvinyl polymers, **cellulose** derivatives such as cellulose acetate, polyamides (nylon 6-10, polyladipyl-L-lysines, polytrephthalamides and poly-(tetraphthaloyl-L-lysines)), poly-α-caprolactam, polydimethylsiloxane, polyesters, poly(ethylene-vinyl acetate), polyglycolic acid, polylactic acid and its copolymers, polylactanic acid, polylysine, polystyrene, shellac, xanthan gum, anionic polymers of methacrylic acid and methacrylic acid esters, **hydroxyalkylcellulose** and mixtures thereof. Particularly preferred texture modifiers are **cellulose**, e.g., carboxymethyl **cellulose** and microcrystalline **cellulose**; polydextrose; modified starch; dextrins; gums, e.g. xanthan, guar, locust-bean, carrageenan and alginates; pectins, maltodextrins and carbomers.

DETD . . . coating of the present invention can be selected, e.g., from the group consisting of acacia gum, alginic acid and alginates,

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carboxymethylcellulose, ethylcellulose, gelatine, **hydroxypropylcellulose, hydroxypropylmethylcellulose, methylcellulose**, xanthan gum, povidone, tragacanth, microcrystalline **cellulose, hydroxyethylcellulose, ethylhydroxyethylcellulose,** sodium **carboxymethylcellulose**, polyethylene glycols, **polyvinylpyrrolidone, polyvinyl** alcohol, polyvinyls acid, gum arabic, lactose, starch (wheat, maize, potato and rice starch), sucrose,
glucose, mannitol, sorbitol, xylitol, stearic acid, hydrogenated cottonseed oil, hydrogenated castor oil, vinylpyrrolidone-vinyl acetate copolymers, fructose, **methylhydroxyethylcellulose**, agar-agar, carrageenan, karaya gum, alginic acid, bentonites and mixtures thereof. Especially preferred materials are plasticizers which can be selected from.

DETD . . . A preferred method to decrease charge on the multiparticulates is by the electrodynamic spraying of a aqueous solution, preferably an conductive **polyvinyl** alcohol aqueous solution, as described in Electrospraying of a highly conductive and viscous liquid, Sparazza et al. Journal of Electrostatics,.

DETD . . . acid, caffeine, **N**-acetylmethadrine, phenylpropanolamine, diphenhydramine, chlorphenisamine, dextromethorphan, berberine, loperamide, mefenamic acid, diclofenamic acid, artemisinin, terfenadine, cartilizine, phenyloin, quinfenazin, N-acetylprocainamide HCl, **pharmaceutically** acceptable salts thereof and derivatives thereof.

DETD [0157] Particularly preferred agents include antibiotics such as clarithromycin, amoxicillin, erythromycin, ampicillin, penicillin, cephalosporins, e.g., cephalexin, **pharmaceutically** acceptable salts thereof and derivatives thereof.

DETD [0158] Other preferred agents are acetaminophen and NSAIDS such as ibuprofen, indomethacin, aspirin, diclofenac and **pharmaceutically** acceptable salts thereof.

DETD . . . dose is dependent on the amount of drug needed to provide the intended therapeutic effect and the amount of any **pharmaceutically** acceptable excipient which may be necessary. Typically, a unit dose of from about 0.02 mg to about 1.5 g would. . .

DETD Controlled-**Release** Ibuprofen 800 mg

DETD . . . bed. The material is then sprayed with the Surelease dispersion

to achieve a 30-70% wt. gain depending on the desired **release** profile at a spraying rate of 1.0 g/min with an atomizing air pressure of 2 bar.

Once the desired weight.

DETD Controlled-**Release** Clarithromycin

DETD . . . KS-100 and KL-100 is prepared, they are mixed at varying ratios

(e.g. 1:3, 1:1 and 3:1) to produce the required **release** profile. With the precision coater module attached the vessel is preheated at 70° C. for 15 minutes with a nominal. . . The material is then sprayed with the Eudragit RS/RL-100 dispersion to achieve a 6-30% wt. gain depending on the desired **release** profile at a spraying rate of 1.0 g/min with an atomizing air pressure of 2 bar.

DETD Controlled-**Release** Erythromycin Coated Clarithromycin

DETD . . . KS-100 and KL-100 is prepared, they are mixed at varying ratios

L57 ANSWER 6 OF 79 USPATFULL on STN (Continued)
B2 U.S.P. criteria (average **release** at 45 minutes in 6.8 pH buffer for 12 units is at least 75%, with none of the 12 units **releasing** less than 60% in 45 minutes) and the Level B1 U.S.P. criteria (average **release** at 45 minutes in 6.8 pH buffer for 24 units is at least 75%, with none of the 24 units **releasing** less than 50% in 45 minutes, and no more than two of the 24 units **releasing** less than 60% in 45 minutes). It should be noted that the pH 6.8 buffer phase drug **release** for this formulation is faster than the corresponding pH 6.8 buffer **release** in the formulation of Example 10.

DETD . . . Type IV apparatus described above in connection with Example 10. A flow rate of 32 ml/min was used. The drug **release** was quantified by UV absorbance measurement at 318 nm. Dissolution studies were performed in both acidic dissolution media (0.1N Hydrochloric. . .

DETD [0372] It is evident from the acid phase **release** shown in FIG. 7 and Table 5 that Sustetric-coated indomethacin can be sprayed coated with PEG6000 without adversely affecting the integrity of the polymer coat. Moreover, the formulation meets the U.S.P. acceptance criteria for "Acid Stage" **release** of "Delayed-release (Enteric-coated) Articles" (Level A1: less than 10% **released** in 2 hours in 0.1 N hydrochloric acid in each of 6 units).

DETD [0374] As shown, the total buffer-phase drug **release** for melt granulated Sustetric-coated indomethacin of Example 2 (i.e., Acryl-ex coated melt granulated indomethacin of Example 2). In particular, only one of the six cells reached 85% drug-**release** in 45 minutes, with an average 45 minute **release** of 72.93%. It is believed that the slow **release** may be attributed to the hydrophobic **release** applied on the granules or a deleterious affect on the polymer coat due.

DETD . . . Type IV apparatus described above in connection with Example 10. A flow rate of 32 ml/min was used. The drug **release** was quantified by UV absorbance measurement at 318 nm. Dissolution studies were performed in both acidic dissolution media (0.1N Hydrochloric.

DETD [0381] As such, this formulation meets the U.S.P. acceptance criteria for "Acid Stage" **release** of "Delayed-release (Enteric-coated) Articles" (less than 10% **released** in 2 hours in 0.1 N hydrochloric acid in each of 6 units (U.S.P. Level A1).

DETD . . . the data in FIG. 10 and Table 6, this formulation would also appear likely to meet the U.S.P. "Buffer Stage" **release** of "Delayed-release (Enteric-coated) Articles". It should be noted that the data does not, in fact pass the Level B1 U.S.P. criteria (85% **released** within 45 minutes in 6.8 pH buffer in each of 6 units). However, it is believed that the formulation would likely meet the Level

L57 ANSWER 6 OF 79 USPATFULL on STN (Continued)
B2 U.S.P. criteria (average **release** at 45 minutes in 6.8 pH buffer for 12 units is at least 75%, with none of the 12 units **releasing** less than 60% in 45 minutes) and the Level B1 U.S.P. criteria (average **release** at 45 minutes in 6.8 pH buffer for 24 units is at least 75%, with none of the 24 units **releasing** less than 50% in 45 minutes, and no more than two of the 24 units **releasing** less than 60% in 45 minutes).

DETD . . . Type IV apparatus described above in connection with Example 10. A flow rate of 32 ml/min was used. The drug **release** was quantified by UV absorbance measurement at 318 nm. Dissolution studies were performed in both acidic dissolution media (0.1N Hydrochloric.

DETD [0392] It should be noted that the acid-phase drug **release** of FIG. 11 and Table 7 shows more variability than in the sustetric coated melt-granulation of Example 12, FIG. 7. . .

DETD [0392] The buffer-phase dissolution profile for this formulation is slow

L57 ANSWER 6 OF 79 USPATFULL on STN (Continued)
(e.g. 1:3, 1:1 and 3:1) to produce the required **release** profile. With the precision coater module attached, the vessel is preheated at 70° C. for 15 minutes with a nominal. . . The material is then sprayed with the Eudragit RS/RL-100 dispersion to achieve a 6-30% wt. gain depending on the desired **release** profile at a spraying rate of 1.0 g/min with an atomizing air pressure of 2 bar.

DETD [0274] Step 3: Overcoating With a **Polyvinylalcohol** (PVA) Based Coating Formulation

DETD Controlled-**Release** Sodium Valproate

DETD . . . bed. The material is then sprayed with the Surelease dispersion

to achieve a 6-30% wt. gain depending on the desired **release** profile at a spraying rate of 1.0 g/min with an atomizing air pressure of 2 bar.

DETD . . . Prior to commencing granulation of the Indomethacin (pulverized), the vessel of an FM Micro fluid bed dryer available from Niro **Pharma** Systems of GEA Niro, Inc.) is pre-warmed by heating at 70° C. for 25 minutes with a nominal airflow of.

DETD [0350] Dissolution testing was then performed using a United States **Pharmacopeia** Type IV dissolution apparatus (Serafarm USP Type IV apparatus), configured to recirculate the dissolution media. More specifically, the apparatus was a Sotax SR 90. A flow rate of 32 ml/min was used. The drug **release** was quantified by UV absorbance measured at 318 nm. Dissolution studies were performed in a Basic dissolution media (45 minutes.

DETD . . . Type IV apparatus described above in connection with Example 10. A flow rate of 32 ml/min was used. The drug **release** was quantified by UV absorbance measured at 318 nm. Dissolution studies were performed in both acidic dissolution media (0.1N Hydrochloric. . . .

DETD [0376] A concern therefore prepping an enteric coated, melt granulated formulation was that the acid phase drug **release** would be unacceptably high, due to a mixing of the enteric coating polymer with the PEG (000 melt kinder. It was postulated that if this occurred, there would be a high degree of drug **release** in the acid phase due to dilution of the polymer coat. To prevent this, a melt binder was selected.

DETD . . . data that the enteric coated melt granulated Indomethacin formulation of step 2 does not exhibit a high degree of drug **release** in the acid phase. To the contrary, less than 1.5% of the formulation dissolved after 2 hours. As such, this formulation meets the U.S.P. acceptance criteria for "Acid Stage" **release** of "Delayed-**release** (Enteric-coated) Articles" (less than 10% **released** in 2 hours in 0.1 N hydrochloric acid in each of 6 units (U.S.P. Level A1)).

DETD [0365] As illustrated in FIG. 6 and Table 4, 78-90% of the indomethacin was **released** within 45 minutes. As such, this formulation would also appear likely to meet the U.S.P. "Buffer Stage" **release** of "Delayed-**release** (Enteric-coated) Articles". It should be noted that the data does not, in fact pass the Level B1 U.S.P. criteria (85% **released** within 45 minutes in 6.8 pH buffer in each of 6 units). However, it is believed that the formulation would likely meet the Level

CLM What is claimed is:
. . . formulation for gastrointestinal deposition comprising a non-compressed free flowing plurality of particles comprising a core comprising a drug and a **pharmaceutically** acceptable excipient, said core overcoated with a functional coating, said drug particles having a mean diameter of greater than 10. . . .

CLM What is claimed is:
9. The formulation of claim 1 wherein said functional coated particles are melt granulated with a **pharmaceutically** acceptable excipient.

CLM What is claimed is:
14. The drug formulation of claim 1 wherein said excipient provides a controlled **release** of the drug upon gastrointestinal deposition.

CLM What is claimed is:
15. The drug formulation of claim 14 wherein said excipient provides a controlled **release** of the drug upon gastrointestinal deposition to provide a therapeutic effect for at least 12 hours after oral administration.

CLM What is claimed is:
16. The drug formulation of claim 14 wherein said excipient provides a controlled **release** of the drug upon gastrointestinal deposition to provide a therapeutic effect for at least 24 hours after oral administration.

CLM What is claimed is:
17. The drug formulation of claim 1 wherein said excipient provides a delayed **release** of the drug upon gastrointestinal deposition.

CLM What is claimed is:
18. The drug formulation of claim 17 wherein said excipient provides a delayed **release** of the drug upon gastrointestinal deposition to effect intestinal absorption.

CLM What is claimed is:
25. The drug formulation of claim 1 wherein said functional coating provides a controlled **release** of the drug upon gastrointestinal deposition.

CLM What is claimed is:
24. The drug formulation of claim 12 wherein said functional coating provides a controlled **release** of the drug upon gastrointestinal deposition to provide a therapeutic effect for at least 24 hours after oral administration.

CLM What is claimed is:
. . . formulation of claim 12 wherein said functional coating provides a controlled **release** of the drug upon gastrointestinal deposition to provide a therapeutic effect for at least 24 hours after oral administration.

CLM What is claimed is:
28. The drug formulation of claim 1 wherein said functional coating

L57 ANSWER 6 OF 79 USPATFULL on STN (Continued)
provides a delayed **release** of the drug upon gastrointestinal deposition.

CLM What is claimed is:
27. The drug formulation of claim 26 wherein said functional coating provides a delayed **release** of the drug upon gastrointestinal deposition to effect intestinal absorption.

CLM What is claimed is:
40. The drug formulation of claim 14 wherein said controlled **release** excipient is a hydrophobic material.

CLM What is claimed is:
. . . drug formulation of claim 42 wherein said hydrophobic material is selected from the group consisting of an acrylic polymer, a **cellulosic** material, shellac, zein and mixtures thereof.

CLM What is claimed is:
46. The drug formulation of claim 42 wherein said controlled **release** excipient is a **cellulosic** material.

CLM What is claimed is:
47. The drug formulation of claim 46 wherein said **cellulosic** material is selected from the group consisting of **cellulose** esters, **cellulose** diesters, **cellulose** triesters, **cellulose** ethers, **cellulose** ester-ether, **cellulose** acrylate, **cellulose** diacylate, **cellulose** triacylate, **cellulose** acetate, **cellulose** diacetate, **cellulose** triacetate, **cellulose** acetate propionate, **cellulose** acetate butyrate and mixtures thereof.
CLM What is claimed is:
48. The drug formulation of claim 17 wherein said delayed **release** material is an enteric polymer.

CLM What is claimed is:
. . . The drug formulation of claim 37 wherein said enteric polymer is selected from the group consisting of **cellulose** esters, **cellulose** acetate phthalate, hydroxypropyl **methylcellulose** acetate succinate, **polyvinyl** acetate phthalate, **cellulose** acetate trimellitate, **carboxymethylcellulose** and mixtures thereof.

CLM What is claimed is:
. . . acrylic acid polymers and copolymers (polyacrylamides, polyacrylimidazines, polyalkyl cyanoacrylates, polymethyl methacrylates), agar-agar, agarose, albumin, alginic acid and alginates, carboxyvinyl polymers, **cellulose** derivatives such as **cellulose** acetate, polyamides (nylon 6-10, poly(sodium)-L-lysines), poly(terephthalamides and poly(N,N'-terephthaloyl-L-lysines)), poly-e-caprolactam, polydimethylsiloxanes, polyesters, poly(ethylene-vinyl acetate), polylysolic acid, polyactic acid and its copolymers, polyglutamic acid,

polylysine, polystyrene, shellac, xanthan gum, anionic polymers of methacrylic acid and methacrylic acid esters, **hydroxyalkylcelluloses** and mixtures thereof.

L57 ANSWER 6 OF 79 USPATFULL on STN (Continued)
functional coating, said drug particles having a mean diameter of greater than 10. . .
CLM What is claimed is:
. preparing a drug formulation comprising a non-compressed free flowing
plurality of particles comprising a core comprising a drug and a **pharmaceutically** acceptable excipient, said core overcoated with a functional coating, said drug particles having a mean diameter of greater than 10. . .
CLM What is claimed is:
83. The formulation of claim 74 wherein said functional coated particles
are melt granulated with a **pharmaceutically** acceptable excipient.

CLM What is claimed is:
88. The method of claim 74 wherein said excipient provides a controlled **release** of the drug upon gastrointestinal deposition.

CLM What is claimed is:
89. The method of claim 88 wherein said excipient provides a controlled **release** of the drug upon gastrointestinal deposition to provide a therapeutic effect for at least 12 hours after oral administration.

CLM What is claimed is:
90. The method of claim 88 wherein said excipient provides a controlled **release** of the drug upon gastrointestinal deposition to provide a therapeutic effect for at least 24 hours after oral administration.

CLM What is claimed is:
91. The method of claim 74 wherein said excipient provides a delayed **release** of the drug upon gastrointestinal deposition.

CLM What is claimed is:
92. The method of claim 91 wherein said excipient provides a delayed **release** of the drug upon gastrointestinal deposition to effect intestinal absorption.

CLM What is claimed is:
97. The method of claim 74 wherein said functional coating provides a controlled **release** of the drug upon gastrointestinal deposition.

CLM What is claimed is:
98. The method of claim 97 wherein said functional coating provides a controlled **release** of the drug upon gastrointestinal deposition to provide a therapeutic effect for at least 12 hours after oral administration.

CLM What is claimed is:
99. The method of claim 97 wherein said functional coating provides a controlled **release** of the drug upon gastrointestinal deposition to provide a therapeutic effect for at least 24 hours after oral administration.

CLM What is claimed is:
100. The method of claim 74 wherein said functional coating provides a delayed **release** of the drug upon gastrointestinal deposition.

CLM What is claimed is:

L57 ANSWER 6 OF 79 USPATFULL on STN (Continued)

CLM What is claimed is:
56. The drug formulation of claim 55 wherein said **hydroxyalkylcellulose** is **hydroxypropylmethylcellulose**.

CLM What is claimed is:
57. The drug formulation of claim 22 wherein said texture modifier is selected from the group consisting of acacia gum, . . . acrylic acid polymers and copolymers (polyacrylamides, polycyrildeatins, polyalkyl cyanoacrylates, polymethyl methacrylates), agar-agar, agarose, albumin, alginic acid and alginates, carboxyvinyl polymers, **cellulose** derivatives such as **cellulose** acetate, polyamides (nylon 6-10, poly(sodium)-L-lysines, polyterephthalamides and poly-(terephthaloyl-L-lysines)), poly-e-caprolactam, polydimethylsiloxanes, polyesters, poly (ethylene-vinyl acetate), polylysolic acid, polyactic acid and its copolymers, polyglutamic acid,

polylysine, polystyrene, shellac, xanthan gum, anionic polymers of methacrylic acid and methacrylic acid esters, **hydroxyalkylcelluloses** and mixtures thereof.

CLM What is claimed is:
. . . wherein said chip resistant coating comprises a material selected from the group consisting of acacia gum, alginic acid and alginates, **carboxymethylcellulose**, **ethylcellulose**, gelatine, **hydroxypropylcellulose**, **hydroxypropylmethylcellulose**, **methylcellulose**, xanthan gum, pectin, tragacanth, microcrystalline **cellulose**, **hydroxyethylcellulose**, methylhydroxyethylcellulose, sodium **carboxymethylcellulose**, polyethylene glycols, **polyvinylpyrrolidone**, **polyvinyl** alcohol, polyacrylic acid, gum arabic, lactose, **starch** (wheat, maize, potato and rice starch), sucrose,

glucose, mannitol, sorbitol, xylitol, stearic acid, hydrogenated cottonseed oil, hydrogenated castor oil, vinylpyrrolidone-vinyl acetate copolymers, fructose, **methylhydroxyethylcellulose**, agar-agar, carrageenan, karaya gum, chitosan, starch hydrolysates and mixtures thereof.

CLM What is claimed is:
. . of a drug formulation comprising a non-compressed free flowing plurality of particles comprising a core comprising a drug and a **pharmaceutically** acceptable excipient, said core overcoated with a functional coating, said drug particles having a mean diameter of greater than 10. . .
CLM What is claimed is:
69. The formulation of claim 63 wherein said functional coated particles
are melt granulated with a **pharmaceutically** acceptable excipient.

CLM What is claimed is:
. . . formulating a drug formulation comprising a non-compressed free flowing plurality of particles comprising a core comprising a drug and a
pharmaceutically acceptable excipient, said core overcoated with a

L57 ANSWER 6 OF 79 USPATFULL on STN (Continued)
101. The method of claim 100 wherein said functional coating provides a delayed **release** of the drug upon gastrointestinal deposition to effect intestinal absorption.

CLM What is claimed is:
116. The method of claim 88 wherein said controlled **release** excipient is a hydrophobic material.

CLM What is claimed is:
. . . The method of claim 116 wherein said hydrophobic material is selected
from the group consisting of an acrylic polymer, a **cellulosic** material, shellac, zein and mixtures thereof.

CLM What is claimed is:
120. The method of claim 116 wherein said controlled **release** excipient is a **cellulosic** material.

CLM What is claimed is:
121. The method of claim 120 wherein said **cellulosic** material is selected from the group consisting of **cellulose** esters, **cellulose** diesters, **cellulose** triesters, **cellulose** ethers, **cellulose** ester-ether, **cellulose** acrylate, **cellulose** diacylate, **cellulose** triacylate, **cellulose** acetate, **cellulose** diacetate, **cellulose** triacetate, **cellulose** acetate propionate, **cellulose** acetate butyrate and mixtures thereof.
CLM What is claimed is:
122. The method of claims 91 and 100 wherein said delayed **release** material is an enteric polymer.

CLM What is claimed is:
. . . 123. The method of claim 122 wherein said enteric polymer is selected
from the group consisting of methacrylic acid copolymers, **cellulose** acetate phthalate, hydroxypropyl **methylcellulose** phthalate, hydroxypropyl **methylcellulose** acetate succinate, **polyvinyl** acetate phthalate, **cellulose** acetate trimellitate, **carboxymethylcellulose** and mixtures thereof.

CLM What is claimed is:
. . . acrylic acid polymers and copolymers (polyacrylamides, polyacrylimidazines, polyalkyl cyanoacrylates, polymethyl methacrylates), agar-agar, agarose, albumin, alginic acid and alginates, carboxyvinyl polymers, **cellulose** derivatives such as **cellulose** acetate, polyamides (nylon 6-10, poly(sodium)-L-lysines, polyterephthalamides and poly-(terephthaloyl-L-lysines)), poly-e-caprolactam, polydimethylsiloxanes, polyesters, poly (ethylene-vinyl acetate), polylysolic acid, polyactic acid and its copolymers, polyglutamic acid,

polylysine, polystyrene, shellac, xanthan gum, anionic polymers of methacrylic acid and methacrylic acid esters, **hydroxyalkylcelluloses** and mixtures thereof.

CLM What is claimed is:
130. The method of claim 129 wherein said **hydroxyalkylcellulose** is **hydroxypropylmethylcellulose**.

CLM What is claimed is:

L57 ANSWER 6 OF 79 USPATFULL on STN (Continued)

131. The method of claim 96 wherein said texture modifier is selected from the group consisting of acacia gum, acrylic acid polymers and copolymers (polyacrylamides, polyacrylonitrile, polyalkyl cyanoacrylates, polymethyl methacrylates), agar-agar, agarose, albumin, alginic acid and alginates, carboxyvinyl polymers, **cellulose** derivatives such as **cellulose** acetate, polyamides (nylon 6:10, poly(adipyl-L-lysine), polyterephthalamides and poly-(terephthalaoyl-L-lysine)), poly-e-caprolactam, polydimethylsiloxane, polyesters, poly (ethylene-vinyl acetate), polyglycolic acid, polylactic acid and its copolymers, polyphosphoric acid,

polypeptide, polystyrene, shellac, xanthan gum, anionic polymers of methacrylic acid and methacrylic acid esters, **hydroxyalkylcelluloses** and mixtures thereof.

CLM What is claimed is:

. . . wherein said chip resistant coating comprises a material selected from the group consisting of acacia gum, alginic acid and alginates, **carboxymethylcellulose, ethylcellulose,** gelatine, **hydroxypropylcellulose, hydroxypropylmethylcellulose, methylcellulose,** xanthan gum, pectin, tragacanth, microcrystalline **cellulose, hydroxyethylcellulose, ethylhydroxyethylcellulose,** sodium **carboxymethylcellulose,** polyethylene glycols, **polyvinylpyrrolidone,** polyvinyl alcohol, polyacrylic acid, gum arabic, lactose, starch (wheat, maize, potato and rice starch), sucrose,

glucose, mannitol, sorbitol, xylitol, stearic acid, hydrogenated cottonseed oil, hydrogenated castor oil, vinylpyrrolidone-vinyl acetate copolymers, fructose, **methylhydroxyethylcellulose,** agar-agar, carrageenan, karaya gum, chitosan, starch hydrolysates and mixtures thereof.

CLM What is claimed is:

. . . surface water coalescence comprising preparing a non-compressed free flowing plurality of particles comprising a core comprising a drug and a

pharmaceutically acceptable excipient, and overcoating said core with a coating exhibiting water coalescence on the surface of said particles.

CLM What is claimed is:

. . . minimal static charge comprising preparing a non-compressed free flowing plurality of particles comprising a core comprising a drug and a

pharmaceutically acceptable excipient, and overcoating said core with a coating which minimizes static charge between said particles.

CLM What is claimed is:

. . . for pharmaceutical deposition comprising preparing a non-compressed

free flowing plurality of particles comprising a core comprising a drug and a **pharmaceutically** acceptable excipient air jet sieving said particles to separate said cores from fine particles; and overcoating said core with a. . .

CLM What is claimed is:

L57 ANSWER 7 OF 79 USPATFULL on STN (Continued)

. . . for gastrointestinal deposition comprising preparing a non-compressed

free flowing plurality of particles comprising a core comprising a drug and a **pharmaceutically** acceptable excipient; and overcoating said core with a functional coating.

CLM What is claimed is:

. . . . to humidity change comprising preparing a non-compressed free flowing

plurality of particles comprising a core comprising a drug and a **pharmaceutically** acceptable excipient; and overcoating said core with a functional coating such that the cohesiveness of said particles does not substantially. . . .

CLM What is claimed is:

165. The method of claim 155 wherein said functional coated particles are melt granulated with a **pharmaceutically** acceptable excipient.

CLM What is claimed is:

171. A controlled **release** formulation comprising a drug and a sufficient amount of a lacquer agent to provide a controlled **release** of the drug. . . .

CLM What is claimed is:

180. The formulation of claim 171 further comprising a channeling agent such as **polyvinylpyrrolidone,** polyethyleneglycol, dextrose, sucrose, mannitol, xylitol, lactose and combinations thereof.

CLM What is claimed is:

. . . deposition comprising a non-compressed free flowing plurality of particles comprising a core comprising chlorpheniramine or a salt thereof and a **pharmaceutically** acceptable excipient, said core overcoated with a functional coating, said particles having a mean diameter of greater than 10 **m**. . . .

L57 ANSWER 7 OF 79 USPATFULL on STN

ACCESSION NUMBER: 2004199812 USPATFULL
TITLE: Process for coating solid particles
INVENTOR(S): Sheskey, Paul J, Midland, MI, UNITED STATES
Kealy, Colin M, Midland, MI, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20040234676	A1	20041125
	US 7070928	B2	20060704
APPLICATION INFO.:	US 2004-494325	A1	20040621 (10)
	WO 2002-US36764		20020823

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-317402P	20010904 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	THE DOW CHEMICAL COMPANY, INTELLECTUAL PROPERTY SECTION, P. O. BOX 1967, MIDLAND, MI, 48641-1967	
NUMBER OF CLAIMS:	17	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Page(s)	
LINE COUNT:	441	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for coating solid particles which comprises the steps of a) contacting a gas with a fluid composition comprising i) a polymer and ii) a liquid diluent to produce a foam, and ii) contacting the produced foam with solid particles and agitating the particles to provide a coating on the solid particles.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM [0001] This invention relates to a process for coating solid particles, particularly drug-containing solid particles, such as **pharmaceutical** tablets, granules and pellets.

SUMM [0002] Coatings are generally applied to solid particles, such as **pharmaceutical** forms, to protect the ingredients against the atmosphere, to mask objectionable tastes and odors, to ease swallowing, to improve. . . .

SUMM [0025] **Methylcellulose** and hydroxypropyl **methylcellulose** have been used for a long time as coating materials for **pharmaceutical** forms. U.S. Pat. No. 3,619,218 discloses that these coating are tacky, uneven, and require extensive polishing after coating. To solve. . . .

ethanol),

from 35 to 45 weight percent of chloroform and from 2 to 5 weight percent of low viscosity methyl **cellulose**. Since the issue of the U.S. patent, the coating technology has progressed and high quality coatings are obtainable without the use of chloroform. However, **methylcellulose** and hydroxypropyl **methylcellulose** are dissolved in water or a mixture of water and alcohol and sprayed on an agitated mass of **pharmaceutical** forms. The spraying technique is a sophisticated process which requires well-defined processing parameters and quite complex equipment

Moreover,

the viscosity of the solutions of **methylcellulose** and hydroxypropyl **methylcellulose** must be low enough that they are still sprayable.

SUMM [0026] U.S. Pat. No. 3,67,764 discusses in detail the disadvantages of spray coating of **pharmaceutical** solid forms, such as the high pressures which are required to sufficiently atomize a coating medium.

L57 ANSWER 7 OF 79 USPATFULL on STN (Continued)

To solve these problems, U.S. Pat. No. 3,67,764 discloses a process for

coating a **pharmaceutical** solid form wherein a foamed viscous sugar medium is applied to the solid surface, the coating medium is then urged. . . .

DETD . . . ghatti, guar gum, exudate gums, seaweed gums, seed gums, microbial gums, carrageenan, dextrin, gelatin, alginates, pectins, starches, polysaccharides, such as **cellulose** ethers or **cellulose** esters, starch derivatives, guar derivatives or xanthan derivatives. Starch derivatives, guar derivatives or xanthan derivatives are described in more detail. . . .

DETD [0013] Preferred polymers are **cellulose** esters or **cellulose** ethers. Preferred **cellulose** esters are carboxy-C.sub.1-C.sub.3-alkyl **celluloses,** such as carboxymethyl **cellulose,** or carboxy-C.sub.1-C.sub.3-alkyl hydroxy-C.sub.1-C.sub.3-alkyl **celluloses,** such as carboxymethyl hydroxyethyl **celluloses.** Preferably, the **cellulose** ethers are C.sub.1-C.sub.3-alkyl **celluloses,** such as **methylcelluloses;** C.sub.1-C.sub.3-alkyl hydroxy-C.sub.1-3-alkyl **celluloses,** such as hydroxyethyl **methylcelluloses,** hydroxypropyl **methylcelluloses** or ethyl hydroxyethyl **celluloses;** hydroxy-C.sub.1-3-alkyl **celluloses,** such as hydroxyethyl **cellulose** or hydroxypropyl **celluloses;** mixed hydroxy-C.sub.1-C.sub.3-alkyl **celluloses,** such as hydroxyethyl hydroxypropyl **celluloses;** or alkoxy hydroxyethyl hydroxypropyl **celluloses,** the alkoxy group being straight-chain or branched and containing 2 to 8 carbon atoms. Most preferably, the fluid composition comprises a water-soluble **cellulose** ether, such as a **methylcellulose** with a methyl molar substitution DS.sub.methloxyl of from 0.5 to 3.0, preferably from 1 to 2.5, or a hydroxypropyl **methylcellulose** with a DS.sub.methoxy of from 0.5 to 3.0, preferably from 1 to 2.5 and a MS.sub.hydroxypropyl of from 0.05 to 2.0, preferably from 0.1 to 1.5. The viscosity of the **cellulose** ether generally is from 1 to 100,000 mPa.multidot.s, preferably from 3 to 10,000 mPa.multidot.s, more preferably from 3 to 5,000.

DETD [0019] Generally polymers 1) are chosen which have surface-active properties. The above-mentioned polymers, particularly water-soluble **cellulose** ethers, are useful as a surfactant in a water-based fluid composition used in one of the purposes of a. . . .

DETD . . . viscous due to the presence of the polymer. In case the fluid film comprises a hydrophilic polymer such as a **cellulose** ether, water is retained in the lamella of the gas bubbles. The drainage of the liquid from the lamellae is a. . . . Gas qualities can be achieved, particularly if the polymer 1) in fluid compositions used for producing the foam is a **cellulose** ether. The foam quality FQ is given in percent at atmospheric pressure and 25.degree. C. and is defined as follows:

DETD . . . The process of the present invention is particularly useful for

coating solid particles containing a drug, that means for solid **pharmaceutical** forms, preferably tablets, granules, pellets, caplets, capsules, lozenges, suppositories, pessaries and implantable dosage forms. The solid particles may comprise known ingredients, such as **pharmaceutical** excipients, for example lactose, dicalcium phosphate, microcrystalline **cellulose,** sugars, minerals, **cellulose** powder, disintegrants, binders, lubricants, colorants, flavorants or combinations thereof.

DETD . . . the present invention. All parts and percentages are by weight unless otherwise indicated. The alkyl and hydroxyalkyl substitutions of the **cellulose** ethers indicated in the examples below are measured and

L57 ANSWER 7 OF 79 USPATFULL on STN (Continued)
calculated according to ASTM D3876. The apparent viscosities indicated in the
DETD [0035] Placebo tablets are produced from 20 weight percent of a microcrystalline **cellulose**, which is commercially available from FMC Corporation under the trademark Avicel PH 102, 79.5 weight percent of fast flow lactose, commercially available from DMV International **Pharma** and Foremost Farms USA under the designation FFL-316, and 0.5 weight percent of magnesium stearate. The composition is compressed into. .
DETD . . . percent of a powder composition in 95 weight percent of water is prepared. The powder composition comprises a hydroxypropyl methyl **cellulose** and is commercially available under the Trademark Opadry Yellow (06F21172), manufactured by Colorcon (West Point, Pa., USA).
DETD . . . percent of a powder composition in 90 weight percent of water is prepared. The powder composition comprises a hydroxypropyl methyl **cellulose** and is commercially available under the Trademark Opadry Pink (YS-1-2132) manufactured by Colorcon (West Point, Pa., USA). From the aqueous. . .
CLM What is claimed is:
6. The process of claim 1 wherein the polymer 1) is a **cellulose** ether or a **cellulose** ester.

CLM What is claimed is:
7. The process of claim 6 wherein the polymer 1) is a water-soluble **cellulose** ether.

CLM What is claimed is:
13. The process of claim 6 wherein the polymer 1) is a **cellulose** ether or a **cellulose** ester.

CLM What is claimed is:
14. The process of claim 5 wherein the polymer 1) is a **cellulose** ether or a **cellulose** ester.

CLM What is claimed is:
15. The process of claim 14 wherein the polymer 1) is a water-soluble **cellulose** ether.

IT 9000-01-5, Gum arabic **9000-07-1**, Carrageenan 9000-28-6, Gum ghatti 9000-30-0, Guar gum 9000-36-6, Karaya gum 9000-65-1, Gum tragacanth 9000-69-5, Pectin 9004-34-6D, **Cellulose**, esters 9004-34-6D, **Cellulose**, ethers 9004-64-0, Dextran, biological studies 9004-65-3, Hydroxypropyl methyl **cellulose** 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 11138-66-2, Xanthan gum
(**coating** of solid drug particles with polymeric foams)
IT **9000-07-1**, Carrageenan
(**coating** of solid drug particles with polymeric foams)

L57 ANSWER 8 OF 79 USPATFULL on STN (Continued)

A1 19990729

SUMM . . . compounds or triclosan), silver protection agents (e.g. benzotriazole), an odorous action (fragrances, perfume), bleaching action/disinfection (chlorine bleaches), odour masking (e.g. **polyvinylpyrrolidone**), anti-coating agents and enzymes for additional purposes (e.g. lipase for removing grease and fat deposits in the dishwasher). However, modern.
SUMM Japanese patent KOKAI 57-74026 discloses a washing aid surrounded by a water-soluble envelope obtained by mixing **polyvinyl** acetal dialkyl aminoacetate and at least one organic acid, which is solid at ambient temperature. This protective envelope serves to.
DETD . . . in the ionic concentration, i.e. ionic concentration-sensitive polymers. For this purpose it is e.g. possible to use the partly hydrolyzed **polyvinyl** acetates (commercially available under the trade names Mowiol® (Clariant) described in EP 284 191 A2 and EP 284 334 A1, which . . .
DETD . . . provided with an envelope in a device for the application of a film coating of the type known in the **pharmaceutical** industry (e.g. obtainable from Lodiger, Hutlin, GS, t aderly and Driam).
DETD . . . ecrs can be provided with a protective coating. It is possible
to use various prior art materials such as e.g. **cellulose**, **cellulose** oderivatives, **polyvinyl** alcohol, **polyvinyl** alcohol derivatives and matures thereof. Although not preferred, when using the ecrs of example 1 such a protective coating was . . . used in all cases and use was made in preferred manner of a 10 wt. % aqueous solution of a **polyvinyl** alcohol, e.g. the **polyvinyl** alcohol Mowiol® 5-88 (Clariant). The quantity of the protective coating applied can be varied by the expert as a function.
DETD . . . is a hemispherical recess of the white or coloured half-tablet.
Subsequently a fixing substance, e.g. an adhesive (e.g. polyethylene glycol, **polyvinyl** ether, **polyvinyl** alcohol, silicate, preferably melted PEG 4000) is applied to the corresponding half-tablet surface and
optionally the clear rinsing agent particle. . .
IT **Polyvinyl** acetals
(dialkylaminoacetates, shells; detergent tablets for use in dishwashing machines)
IT **9000-07-1**, Carrageenan 26222-40-2, Styrene-4-vinylpyridine copolymer 39388-39-1D, acetals 64798-25-1D, polymers 102499-90-1, 2-(Dimethylamino)ethyl methacrylate-N-[3-(dimethylamino)propyl]methacrylamide-methyl methacrylate copolymer
(**shells**; detergent tablets for use in dishwashing machines)
IT **9000-07-1**, Carrageenan
(**shells**; detergent tablets for use in dishwashing machines)

L57 ANSWER 9 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2004:125182 USPATFULL
TITLE: Composition for use in a dishwashing machine
INVENTOR(S): Wesenhenkel, Guido, Gahlaad, NJ, United States
Windemann, Ralf, Grieheim, GERMANY, FEDERAL REPUBLIC OF
Carbonell, Enric, Barcelona, SPAIN
Hertling, Ludwig, Biblis, GERMANY, FEDERAL REPUBLIC OF
Daschner, Natascha Wolf, Ludwigshafen, GERMANY, FEDERAL
REPUBLIC OF
PATENT ASSIGNEE(S): Reckitt Benckiser N.V., Hoofddorp, NETHERLANDS (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6900190	B1	20041005
APPLICATION INFO.:	WO 2000DO6488		20000210 <---
	US 2002-744726		20020710 (9)
	WO 1999-IT34		19990729 <---

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1999-19834182	19990729 <---
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Hoopes, Lorna M.	
LEGAL REPRESENTATIVE:	Akin Gump Strauss Hauer & Feld, L.L.P.	
NUMBER OF CLAIMS:	47	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 3 Drawing Page(s)	
LINE COUNT:	2189	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

AB Composition for use in a water tank in the kitchen or sanitary sectors characterized by a basic composition essentially evolving its function following addition to a first water filling of the water tank, in the form of a tablet and at least one particle, with at least one core, which comprises at least one substance involving its function essentially following an at least partial emptying of the first water filling from the water tank Ad and the inflow of fresh water and a covering substantially completely surrounding the core or more comprising at least one compound, whose solubility increases with decreasing concentration of a specific ion in the surrounding medium, the at least one particle being so arranged in or on the tablet that the surface of the particle or particles is at most only partly in direct contact with the surface of the basic composition surrounding the same and the concentration of the specific ion in the local environment of the particle or particles is sufficiently high up to a substantially complete dissolving of the tablet in order to prevent a substantial dissolving of the covering or a substantial detachment of the covering from the core or cores.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L57 ANSWER 10 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2004:177879 USPATFULL
TITLE: Edible coating composition
INVENTOR(S): Angelio, Michael, Marlboro, NJ, UNITED STATES
Dell, Sheila M., New Hope, PA, UNITED STATES
Tsaoun, Dominga C., Bensalem, PA, UNITED STATES
Modliszewski, James J., Brick, NJ, UNITED STATES
Farnum, Thomas A., Hockessin, DE, UNITED STATES
Werner, David E., West Grove, PA, UNITED STATES
PATENT ASSIGNEE(S): FMC Corporation (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20040115043	A1	20040715
APPLICATION INFO.:	US 2003-740321	A1	20031218 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2002-145021, filed on 7 Jun 2002, GRANTED, Pat. No. US 6709713 Continuation of Ser. No. US 2000-491724, filed on 27 Jan 2000, GRANTED, Pat. No. US 6432448		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-119805P	19990208 (60) <---
	US 1999-133892P	19990507 (60) <---
	US 1999-134814P	19990519 (60) <---
	US 1999-167407P	19991124 (60) <---
	US 1999-172526P	19991217 (60) <---
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	WOODCOCK WASHBURN LLP, ONE LIBERTY PLACE, 46TH FLOOR, 1650 MARKET STREET, PHILADELPHIA, PA, 19103	
NUMBER OF CLAIMS:	46	
EXEMPLARY CLAIM:	1	
LINE COUNT:	1524	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

AB An edible, hardenable **coating** composition containing microcrystalline **cellulose** and **carrageenan** and either a strengthening polymer, a plasticizer or both. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable **coating** composition containing microcrystalline **cellulose** and **carrageenan** and either a strengthening polymer, a plasticizer or both. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

SUMM [0002] This invention relates to edible, hardenable, prompt **release** **coating** compositions comprising microcrystalline **cellulose**, **carrageenan** and at least one of a strengthening polymer or a plasticizer. The coatings of the present invention can be applied to

L57 ANSWER 9 OF 79 USPATFULL on STN (Continued)
pharmaceutical, including nextraceutical, and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets,
and granules, and foods, are readily. . . media, and, when applied as
a coating and ingested by, for example, a human, do not significantly retard or extend **release** of active ingredient(s) from a substrate coated therewith.
SUM@ [0027] It is a common practice to coat **pharmaceutical** and veterinary tablets to obtain several advantages. Among these are to mask unpleasant
tasting active ingredients with a barrier coat,
SUM@ [0044] Another very important function of a **pharmaceutical** or veterinary tablet coating is to control the integrity of the tablet itself. Uncoated tablets are often subject to being.
SUM@ [0052] Currently, most commercially available edible coatings utilize a synthetic **cellulosic** polymer such as **hydroxypropylmethylcellulose** (HPMC). Other synthetic film-formers which are commonly used include **ethylcellulose, methylcellulose, polyvinylpyrrolidone**, and polyethylene. These polymers may be applied to substrates alone or in combination with secondary film-formers such as sodium alginate or.
SUM@ . . . proportion to the increase in disintegration time. Many other agents commonly used in coating compositions are also known to delay **release** of **pharmaceutical** agents, such as enteric coatings which use polymeric film formers insoluble at low pH but soluble in water, or gastric fluid, some of these being specifically selected to by-pass both
the stomach and small intestine and provide colonic release
SUM@ [0013] The coatings of this invention meet U.S. **Pharmacopeia** standards for rapid or immediate dissolution (U.S.P., monograph 23) of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablet or other substrates. Thus, they do not adversely impact or retard **release** of active ingredients from a substrate coated with them. Further, the coatings of this invention are readily dispersed and rapidly.
SUM@ . . . with the present invention, a coating composition which comprises a unique combination of materials specifically adapted for a prompt **release** when placed aqueous media or ingested by, e.g., by a human. The coating composition of the present invention comprises microcrystalline **cellulose**, microcrystalline **cellulose** gel, at least one of a strengthening polymer and a plasticizer. More specifically, the present invention provides a prompt **release**, edible, hardenable **coating** composition comprising microcrystalline **cellulose** and **carrageenan**, and at least one of strengthening polymer or plasticizer, preferably both, as well as to dry coatings and aqueous dispersions.
SUM@ [0016] The present invention also provides **pharmaceutical**, including nextraceutical, and veterinary solid dosage forms, confectionery, seeds,
animal feed, fertilizers, pesticide tablets and granules, and foods coated with the propel amounts of edible, hardenable coatings of this invention.
DETD . . . application, the term "edible" is intended to mean food grade

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materials which are approved by regulatory authorities for use in **pharmaceutical** or food applications. The term "hardenable" used to describe the coating compositions of the present invention is intended to include only. . . . that can be handled and packaged but which do not resist abrasive forces significantly. The terms "immediate", "rapid" or "prompt" **release** as applied to dissolution rates or times for the coating compositions of this invention or tablets coated with the compositions of this invention mean that the coatings of this invention
meet U.S. **Pharmacopeia** standards (U.S.P. monograph 23) for rapid or immediate dissolution of active ingredients from tablets or other solid dosage forms coated therewith. Thus, they provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablet or other substrates. The term do not, consistent with the **pharmacopeia** standards above, when placed in aqueous media or ingested by, e.g., a human significantly impede or retard **release** or dissolution of tablets or other solid dosage forms coated therewith. For example, coatings made in accordance with the present . . . completely disintegrated and/or dissolved within less than 10 minutes after being ingested or placed in aqueous media. Thus, when a **pharmaceutical** solid dosage form is coated with the coating of this invention and ingested by a human or other animal, the ...
DETD [0017] The microcrystalline **cellulose**, either coprocessed with carrageenan or simply blended therewith, interacts with the carrageenan to provide important film-forming characteristics required to provide an
elegant coating which is particularly useful in, for example, coating **pharmaceutical** and veterinary tablets, granules, and spheres which contain active ingredients which require **release** promptly after being placed in aqueous media or ingested.
DETD [0018] Microcrystalline **cellulose** is a purified, partially depolymerized **cellulose** that is generally prepared by treating a source of **cellulose**, preferably alpha **cellulose** in the form of a pulp from fibrous plants, with a mineral acid, preferably hydrochloric acid. The acid selectively attacks the less ordered regions of the **cellulose** polymer chain. Thereby exposing and freeing the crystalline sites, forming the crystallite aggregates which constitute microcrystalline **cellulose**. These crystallites are separated from the reaction mixture and washed to remove degraded by-products. The resulting wet mass, generally containing 40 to 60% moisture, is then dried. As noted to in the art by several names, including hydrolyzed **cellulose**, microcrystalline **cellulose**, microcrystalline **cellulose** gel, or simply wetcake. This microcrystalline **cellulose** wetcake may be used as such or may be further modified, for example, by attrition and/or drying, and utilized in.
DETD [0019] Microcrystalline **cellulose** may also be produced for use in the present invention using a steam explosion treatment. In this process, wood chips or other **cellulosic** materials are placed in a chamber into which super-heated steam is introduced. After being maintained for a period of about 1-5 minutes, the exit valve is released rapidly, **releasing** the contents explosively and yielding microcrystalline **cellulose**. No additional acid need be introduced during the explosion mixture, since it is believed that the acidic materials in the wood chips and the elevated temperature and pressure hydrolyze the

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coprocessed microcrystalline **cellulose**/carrageenan.
DETD . . . thereof is spread on a surface and allowed to dry. However, the
film is considered to be too weak for **pharmaceutical** tablets as shown by the results in Comparative Example A and therefore requires the presence of microcrystalline **cellulose** for satisfactory results.
DETD [0028] A dry, physical blend of lota carrageenan and microcrystalline **cellulose** (Avicel® PH-302, average particle size 180 microns) also yielded what appear to be unsatisfactory films as shown by results in Comparative Example B. Thus, for commercial purposes, it is believed that the average particle size of the microcrystalline **cellulose** used in a dry blend with the natural, film forming hydrocolloid should be below 150 microns, advantageously below about 100 microns, for performance coating formulations within the scope of this invention may be prepared from dry, physical blends of microcrystalline **cellulose** and carrageenan.
DETD [0029] The weight ratio of microcrystalline **cellulose** to carrageenan in the compositions of this invention may vary depending on the application, but generally range from about 90:10 . . . different ratios of coprocessed material. Thus, the dry, physical blends provide significantly greater flexibility for specific applications using different requirements. **Pharmaceutical** and veterinary solid dosage forms containing active ingredients which may require increased carrageenan content in the composition to ideally coat the tablets. For these **pharmaceutical** and veterinary applications, a preferred weight ratio of microcrystalline **cellulose** to carrageenan is in the range of about 75:25 to about 25:75.
DETD [0031] Regardless of whether the composition is based on coprocessed microcrystalline **cellulose**/carrageenan or a dry, physical blend of microcrystalline **cellulose** and carrageenan, a strengthening polymer, preferably **hydroxypropylcellulose**, a plasticizer or both a strengthening polymer and a plasticizer are present in the coating formulation of this invention. The strengthening
DETD [0032] Other strengthening polymers which can provide the same benefit and may be used instead of HPC include HPMC, **hydroxypropylcellulose, ethylcellulose, methylcellulose** and **polyvinylpyrrolidone** (PVP); however, care must be exercised in the use of such alternative materials
to avoid significantly retarding **release** of active ingredients and/or bioavailability. The preferred amount of strengthening polymer is less than the total amount of microcrystalline **cellulose** and carrageenan present in the coating composition. Depending on the desired hardness of the coating, the strengthening polymer may be employed. . . polymer is included in the formulation. Strengthening polymers suitable for use in this invention and which will not significantly retard **release** from tablets or other solid dosage forms are those polymers having a viscosity equal to or less than 20 mPa.multidot.s.
DETD . . . following optional ingredients are also contemplated and within
the scope of the coating compositions of the present invention. The prompt **release** coating compositions of the invention may include at least one filler. Such fillers may include, for example, calcium carbonate, disolcium . . . carbohydrates, such as starch, maltodextrin, lactose, mannitol and other sugars. Of these,
maltodextrin
and mannitol are preferred fillers. The prompt **release** coating compositions of the invention may include at least one surfactant. Such surfactants include either anionic or nonionic surfactants. Useful.

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DETD . . . basis a preferred composition of this invention comprises at least about 47%, suitably about 50% and about 75% of microcrystalline **cellulose** and carrageenan powder combined, more preferably about 65% to about 66%; about 0.5% to about 30% of strengthening polymer, more.

DETD . . . may be preferable to maintain agitation of the aqueous dispersion during the entire period of its being sprayed onto the **pharmaceutical** or veterinary solid dosage form; confectionery, seeds, animal feed, fertiliser, pesticide tablets, or food.

DETD [0079] The preferred edible, permeable, prompt **release** coating formulations of this invention may generally be prepared and used according to a simple procedure. A dry mixture of carrageenan microcrystalline **cellulose**/carrageenan powder or a dry blend of microcrystalline **cellulose**/carrageenan powder and a strengthening polymer, such as **hydroxyethylcellulose**, polyethylene glycol or other acceptable plasticizer, optionally together with a solid filler such as maltodextrin, lactose, mannitol or the like, .

DETD [0084] In the formulations of microcrystalline **cellulose** and iota carrageenan, a simple propeller mixer provides adequate agitation for rapid hydration. The period of hydration may be . . . thixotropic behavior of a formulation which sets up during overnight storage.

Unlike

coating formulations based primarily on hydroxyalkyl ethers of **Cellulose**, for example, HPMC, consist entirely of the microcrystalline and carrageenan-based formulations of this invention does not need to be hot sprayed.

DETD . . . Engineering. Equipment variables which one skilled in the art can manipulate to provide an elegant coating based on the microcrystalline **cellulose** and carrageenan materials, either hypercreased or dry hypercreased, include inlet temperature, outlet temperature, air flow, speed of rotation of the.

DETD [0064] **Hydroxyethylcellulose** binds water more effectively than carrageenan does. Thus, the presence of the major amount of carrageenan in the formulations of. . . the carrageenan tends to offset the negative effect of HEC on drying time. Thus, in the case of low melting active **pharmaceutical** ingredients (Ingredient), the drying temperature can be reduced and still provide short enough drying time

to

be commercially.

DETD [0063] **Hydroxyethylcellulose** is particularly susceptible to clogging spray nozzles at high temperatures. An additional benefit provided by the formulations of this invention, .

DETD [0044] The level of coating applied to **pharmaceutical** or veterinary dosage forms is preferably between about 0.1% to about 8% by weight of the uncoated dosage form, more.

DETD . . . to those of the uncoated tablets used as a substrate for coating. This is an additional unexpected benefit of the **coatings** based on **carrageenan** and microcrystalline **cellulose**, and it differs from the known drawbacks of HPMC.

DETD [0048] All components of the formulation are typically **pharmaceutically** acceptable, edible food grade materials.

DETD [0051] In a Patterson-Kelley twin shell blender were placed 14.43 grams

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DETD of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 18.36 grams of polyvinylpyrrolidone (PVP32) (GAF), 36.40 grams of polyethylene glycol 8000 (Union Carbide Corporation), and 0.2 grams of yellow #5 food color. After

DETD [0052] by the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250 L, Hercules Incorporated), 10.40 grams of polethylene glycol 8000, and 0.30 gram of yellow #5 food color was.

DETD [0053] By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250 L, Hercules Incorporated), 5.40 grams of polyethylene glycol 8000, 5.0 grams of Micro Talc, and 0.30 gram of

DETD [0054] By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250 L, Hercules Incorporated), 10.40 grams of polethylene glycol 8000, and 0.30 gram of yellow #5 food color was.

DETD [0055] By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250 L, Hercules Incorporated), 10.40 grams of polethylene glycol 8000, 0.30 gram of yellow #5 food color, and 0.30 gram of . . . neutral solution was sprayed using a Vector High Coater LDCS onto 1 Kg of cores comprised of 20% microcrystalline **cellulose** and 80% calcium carbonate, each weighing on average 1.05 grams. Conditions used include an inlet temperature of 70-80° C., and

DETD [0056] By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 10.65 grams of polepthylene glycol 8000, and 0.30 gram of yellow #5 food color was added to 2000 g. and of sucrose . . . and stirred

DETD while it was sprayed using a Vector High Coater LDCS onto 1 Kg of the same cores of microcrystalline **cellulose** and calcium carbonate that were coated in Example 5. Conditions used include an inlet temperature of 78-79° C., and . . . in perlited water at 37° C. was less than 3 minutes. This coating was as robust as coatings containing **hydroxyethylcellulose**.

DETD [0057] By the method of Example 1 a dry mixture of 20.95 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota carrageenan (70:30), 0.55 gram of **hydroxyethylcellulose** (Aqualon® 250 L), 8.140 grams of polyethylene glycol 8000, and 0.30 gram of yellow iron oxide was added to 450 grams . . . solution was continuously stirred while it was sprayed using a Vector High Coater LDCS onto 1.03 Kg of compressed microcrystalline **cellulose** cores (Avicel® PH-200) dewetted with an FMC logo, each weighing on average 0.267 gram. Conditions used include an inlet temperature.

DETD [0058] By the method of Example 1 a dry mixture of 280.75 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (90:10), 7.5 grams of **hydroxyethylcellulose** 250 L, 154.0 grams of polyethylene glycol 8000, and 4.0 grams of hydrophilic red iron oxide was prepared. A portion . . . have as elegant an appearance as those prepared in Examples 1 through 7 in which the 70:30 combination of

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DETD of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (21.0 grams), 22.5 grams of **hydroxyethylcellulose** (Aqualon® 250 L), 28.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), 10.0 grams of a red dye blend (Warner . . .

DETD [0060] In a large Patterson-Kelley twin shell blender were placed 1.940 Kg of a blend of microcrystalline **cellulose** (Avicel® PH-105, 1.358 Kg) and iota carrageenan (0.582 Kg), 0.436 Kg of **hydroxyethylcellulose** (Aqualon® 250 L), 0.277 Kg of maltodextrin (Maltrin® M-180, Grain Processing Corporation), and 1.307 Kg of polyethylene glycol 8000 (Union.

DETD [0070] In a Patterson-Kelley twin shell blender were placed 72.80 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 56 .19 grams) and iota **carrageenan** (16.55 grams), 33.08 grams of **hydroxyethylcellulose** (Aqualon® 250 L), and 44.42 grams of hydrophilic red iron oxide. After being thoroughly mixed, the dry components were added .

DETD [0071] In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (18.0 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250 L), 15.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), and 22.5 grams of hydrophilic yellow oxide. After

DETD [0072] In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (18.0 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250 L), and 21.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation). Simultaneously 22.5 grams of titanium dioxide was.

DETD [0073] In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (18.0 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250 L), 15.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation). Simultaneously 31.0 grams of titanium dioxide was.

DETD [0074] In a Patterson-Kelley twin shell blender were placed 78.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (22.5 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250 L), and 9.0 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation). Simultaneously 30.0 grams of titanium dioxide was.

DETD [0075] In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 49.94 grams) and iota **carrageenan** (16.21 grams), 16.01 grams of **hydroxyethylcellulose** (Aqualon® 250 L), 48.05 grams of polyethylene glycol 8000 (Union Carbide Corporation), 8.19 grams of maltodextrin (Maltrin M-180, Grain Processing.

DETD [0076] In a Patterson-Kelley twin shell blender were placed 78.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (22.5 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250 L), and 1.5 gram of stearic acid. Simultaneously 37.5 grams of titanium dioxide was added to 1516.7 grams.

DETD [0077] In a Patterson-Kelley twin shell blender were placed 300 grams of

a blend of microcrystalline **cellulose** (Avicel® PH-105, 200 grams) and iota **carrageenan** (100 grams), and 100 grams of polyethylene glycol 8000 (Union Carbide Corporation). After the dry

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components had been thoroughly blended, the entire blend was. . .
DETD [0079] In a Patterson-Kelley twin shell blender were placed 49.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 24.2 grams) and iota **carrageenan** (**14**.7 grams), **11**.0 grams of **hydroxyethylcellulose** (Aqualon® 250 L), 33.0 grams of polyethylene glycol 8000 (Union Carbide Corporation), 7.0 grams of maltodextrin (Maltrin M-180, Grain Processing.
DETD [0080] In a Patterson-Kelley twin shell blender were placed 47.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 33 grams) and iota **carrageenan** (**12** grams), **29** grams of **hydroxyethylcellulose** (Aqualon® 250 L), 29.0 trams of triacetin, 4.0 grams of propylene glycol alginate, and 3 grams of Pluronic F-68 (BASF). . .
DETD . . . was prepared by dry blending to provide a coating composition having the following formulation:

Ingredient	Amount (g)
Microcrystalline **cellulose** (Avicel PH-**105**)	37.5
Iota **carrageenan**	**14**.7
Polyethylene glycol 8000	34
Hydroxyethylcellulose 250 L	11
Maltodextrin M-180	3

DETD . . . formulations shown in the following table:

	Example: 31	32	33
	Weight (grams)		
Avicel PH-101	38	34.3	34.3
Iota **carrageenan**	**11**	**14**.7	**14**.7
Hydroxyethylcellulose	--	11	11
POA.sup.a	7		
PEG.sup.b	34	33	33
Lecithin.sup.c	7	4	7
Maltrin M-180	3	3	

.sup.aPropyleneglycol alginate (Protonal **8**. . .
DETD . . . example were dry blended to provide the dry coating composition shown in the following table:

Weight (grams)	
Avicel PH-**105**	33
Iota **carrageenan**	**10**
Hydroxyethylcellulose	**20**

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microcrystalline **cellulose** to carrageenan is in the range of about 90:10 to about 60:40.

CLM What is claimed is:
17. The coating composition of claim 1, wherein the microcrystalline **cellulose** has an average particle size in the range of 1 to 50 microns.

CLM What is claimed is:
18. The coating composition of claim 17, wherein the microcrystalline **cellulose** has an average particle size in the range of about 1 to about 50 microns.

CLM What is claimed is:
20. A dry coating composition comprising a dry blend of microcrystalline **cellulose**, carrageenan and at least one of a strengthening polymer and a plasticizer.

CLM What is claimed is:
21. The coating composition of claim 1 or 20, comprising at least 63% by weight of microcrystalline **cellulose** and carrageenan, from about 0.5% to about 30% strengthening polymer, optionally comprising, about 25% to about 40% plasticizer.

CLM What is claimed is:
22. A coating composition of claim 21, comprising by weight about 45% to about 60% microcrystalline **cellulose** and carrageenan, about 7% to about 22% strengthening polymer, and about 31% to about 35% plasticizer.

CLM What is claimed is:
23. The coating composition of claim 22, wherein the strengthening polymer is **hydroxyethylcellulose** and the plasticizer is selected from the group consisting of polyethylene glycol and triacetin.

CLM What is claimed is:
24. An aqueous dispersion comprising a coating composition of the edible, hardenable, prompt **release** coating composition of claim 1.

CLM What is claimed is:
27. An aqueous dispersion of a composition of claim 1, 2, or 3, wherein said microcrystalline **cellulose** and carrageenan are present in a weight ratio of about 70:30; said strengthening polymer is selected from the group consisting of **hydroxyethylcellulose**, **hydroxypropylmethylcellulose**, **methylcellulose**, **ethylcellulose**, **hydroxypropylcellulose** and **polyvinylpyrrolidone**; said plasticizer is selected from at least one of the group consisting of polyethylene glycol, triacetin, dibutyl sebacate, propylene glycol. . .
CLM What is claimed is:
28. An aqueous dispersion of a composition of claim 19, wherein said microcrystalline **cellulose** and carrageenan are present in a weight ratio of about 70:30

CLM What is claimed is:
29. A **pharmaceutical** or veterinary solid dosage form coated with an

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PGA.sup.a 4
Pluronic F-68 3

.sup.aPropyleneglycol alginate (Protonal ® ester SD-LK, Pronova)
DETD . . . tablets which were tested for friability. This example is summarized in the following table:

Ingredient	Weight (grams)
Avicel PH-**105**	33
Iota **carrageenan**	**14**.5
Hydroxyethylcellulose	**22**
Mannitol.sup.a	15.5
Pluronic F-68	3
Blue Lake #2	8
Deionized water	1150
Hydration time	1 kg
Caplets	
Ibuprofen	
Acetaminophen.	

DETD [0094] A dispersion of 9.70 grams of microcrystalline **cellulose** (Avicel® PH-102, FMC Corporation) and 20.7 grams of iota carrageenan (Viscarin® SD-389) in 1700 grams of deionized water was prepared. .

CLM What is claimed is:
1. An edible, hardenable, prompt **release** coating composition comprising (a) microcrystalline **cellulose**, (b) a film forming amount of carrageenan, and (c) at least one of a strengthening polymer and a plasticizer, wherein said coating composition does not, when ingested or placed in an aqueous medium, significantly retard **release** of active ingredients from a substrate to which said coating is applied.

CLM What is claimed is:
2. The coating composition of claim **1**, wherein the **carrageenan** is iota carrageenan.

CLM What is claimed is:
4. The coating composition of claim 3, wherein said strengthening polymer is selected from the group consisting of **hydroxyethylcellulose**, **hydroxypropylmethylcellulose**, **hydroxypropylcellulose**, **ethylcellulose**, **methylcellulose**, and **polyvinylpyrrolidone**.

CLM What is claimed is:
5. The coating composition of claim 3, wherein the strengthening polymer is **hydroxyethylcellulose**.

CLM What is claimed is:
15. The coating composition of claim 1, wherein the weight ratio of

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edible, hardenable, prompt **release** coating composition of claim 1.

CLM What is claimed is:
30. The **pharmaceutical** or veterinary solid dosage form of claim 29, wherein the coating is applied to the dosage form at a. . .
CLM What is claimed is:
31. The **pharmaceutical** or veterinary solid dosage form of claim 30, wherein the coating is applied to the dosage form at a level. . .
CLM What is claimed is:
32. A **pharmaceutical** or veterinary tablet coated with the aqueous dispersion of claim 28.

CLM What is claimed is:
34. A coating composition for use in lieu of a sugar **coating** consisting of microcrystalline **cellulose**, **carrageenan**, and polyethylene glycol.

CLM What is claimed is:
35. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, high molecular weight polyethylene glycol and maltodextrin, wherein said microcrystalline **cellulose** has a particle size less than 50 microns.

CLM What is claimed is:
36. A **pharmaceutical** solid dosage form comprising the edible coating composition of claim 35.

CLM What is claimed is:
38. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, mannitol, a surfactant and a coloring agent, wherein said microcrystalline **cellulose** has a particle size less than 50 microns.

CLM What is claimed is:
39. A **pharmaceutical** solid dosage form comprising the edible coating composition of claim 38.

CLM What is claimed is:
41. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, and a coloring agent, wherein said microcrystalline **cellulose** has a particle size less than 50 microns. . .

CLM What is claimed is:
42. A **pharmaceutical** solid dosage form comprising the edible coating composition of claim 41.

CLM What is claimed is:
46. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, high molecular weight polyethylene glycol and a coloring agent, wherein said microcrystalline **cellulose** has a particle size less than 50 microns.

CLM What is claimed is:
48. A dry **coating** composition comprising microcrystalline **cellulose**, **carrageenan** and at least one of a strengthening polymer and a plasticizer, wherein said dry composition can be hydrated in a. . .

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L57 ANSWER 10 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2004:109937 USPATFULL
TITLE: Composition for use in a dishwasher
INVENTOR(S): Waschenbach, Guido, Oakland, NJ, United States
Wiedemann, Ralf, Grieshein, GERMANY, FEDERAL REPUBLIC OF
Carbonell, Enric, Barcelona, SPAIN
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Wolf, Natascha, Alt-g, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S): Reckitt Benckiser N.V., Hoofddorp, NETHERLANDS (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6730646	B1	20040504	
	WO 2000006694		20000210	<--
APPLICATION INFO.:	US 2001-744727		20010404 (9)	<--
	WO 1999-EP5265		19990727	<--

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1998-19834180	19980729 <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Douyon, Lorna M.	
LEGAL REPRESENTATIVE:	Akin Gump Strauss Hauer & Feld LLP	
NUMBER OF CLAIMS:	42	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 3 Drawing Page(s)	
LINE COUNT:	1154	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a composition for use in a dishwasher which is provided in the form of a tablet. The inventive composition is characterized by a base composition which essentially carries out its function during the main cleaning cycle of the dishwasher, and is also characterized by at least one particle. Said particle has at least one core that comprises at least one substance which essentially carries out its function during the rinse cycle of the dishwasher. The particle also has a coating which, for the most part, completely surrounds the core(s). Said coating comprises at least one compound whose solubility increases with a declining concentration of a specific ion in the surrounding medium. The at least one particle is arranged in or on the tablet in such a way that the surface of the particle(s) is, at most, partially in direct contact with the surface of the base composition surrounding this/these particles. In order to prevent the coating from substantially dissolving or to prevent the coating from substantially detaching from the core(s), the concentration of the specific ion in the local surrounding of the particle(s) is sufficiently high until the tablet has, for the most part, completely dissolved. The invention also relates to a method for conducting a dishwashing cycle in a dishwasher while using the inventive composition.

L57 ANSWER 10 OF 79 USPATFULL on STN (Continued)

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AI 19990729

SUMM . . . compounds or triclosan), silver protection agents (e.g. benzotriazole), an odorous action (fragrances, perfume), bleaching action/disinfection (chlorine bleaches), odour masking (e.g. **polyvinylpyrrolidone**), anti-coating agents and enzymes for additional purposes (e.g. lipase for removing grease and fat deposits in the dishwasher). However, modern . . .

SUMM Japanese patent KOKAI 50-77406 discloses a washing aid surrounded by a water-soluble envelope obtained by mixing **polyvinyl** acetal dialkyl aminoacetate and at least one organic acid, which is solid at ambient temperature. This protective envelope serves to . . .

DETD . . . in the ionic concentration, i.e. ionic concentration-sensitive polymers. For this purpose it is e.g. possible to use the partly hydrolyzed **polyvinyl** acetates (commercially available under the trade names Mowiol® (Clariant) described in EP 284 191 A2 and EP 284 334 A1, which . . .

DETD . . . provided with an envelope in a device for the application of a film coating of the type known in the **pharmaceutical** industry (e.g. obtainable from Lodiger, Rottlin, GS, Manesty and Driam). . . .

DETD . . . cores can be provided with a protective coating. It is possible to use various prior art materials such as e.g. **cellulose, cellulose** derivatives, **polyvinyl** alcohol, **polyvinyl** alcohol derivatives and mixtures thereof. Although not prescribed, when using the cores of example 1 such a protective coating was . . . used in all cases and use was made in preferred manner of a 10 wt.-% aqueous solution of a **polyvinyl** alcohol, e.g. the **polyvinyl** alcohol Mowiol® 5-88 (Clariant). The quantity of the protective coating applied can be varied by the expert as a function of . . .

DETD . . . in a hemispherical recess of the white or coloured half-tablet. Subsequently a fixing substance, e.g. an adhesive (e.g. polyethylene glycol, **polyvinyl** ether, **polyvinyl** alcohol, silicate, preferably melted PEG 4000) is applied to the corresponding half-tablet surface and . . . optionally the clear rinsing agent particle. . .

IT **Polyvinyl** acetals
(diethylaminoacetate esters; detergent tablets for use in dishwashers)

IT **9000-07-1**, Carrageenan 26222-40-2, Styrene-4-vanylpyridine copolymer 39388-29-1D, acetals 258459-81-1
(Uses), detergent tablets for use in dishwashers)

IT **9000-07-1**, Carrageenan
(Uses), detergent tablets for use in dishwashers)

L57 ANSWER 11 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2004:103724 USPATFULL
TITLE: Composition for use in a laundry washing machine
INVENTOR(S): Waschenbach, Guido, Oakland, NJ, United States
Wiedemann, Ralf, Grieshein, GERMANY, FEDERAL REPUBLIC OF
Carbonell, Enric, Barcelona, SPAIN
Robinson, Paul W., North Ferriby, UNITED KINGDOM
Cordellina, Antonio, I-Abano, ITALY
Bosco, Manuela, Cartagodie di Pasre, ITALY
Franzolin, Giorgio, Scaltenigo, ITALY
Clotet, Joan, Barcelona, SPAIN
Zamuner, Dora, Venice, ITALY
PATENT ASSIGNEE(S): Reckitt Benckiser N.V., Hoofddorp, NETHERLANDS (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6727216	B1	20040427	
	WO 2000006689		20000210	<--
APPLICATION INFO.:	US 2001-744723		20010404 (9)	<--
	WO 1999-7835		19990729	<--

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1998-19834181	19980729 <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Douyon, Lorna M.	
LEGAL REPRESENTATIVE:	Akin Gump Strauss Hauer & Feld LLP	
NUMBER OF CLAIMS:	42	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	6 Drawing Figure(s); 2 Drawing Page(s)	
LINE COUNT:	1067	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a composition for use in a washing machine. The composition is characterized by a base composition that becomes active essentially during the main wash cycle of the washing machine; and by at least one particle with at least one core which contains at least one substance which becomes active essentially during the rinse cycles of the washing machine and with a coating which essentially fully encloses the core(s) and contains at least one compound whose solubility increases as the concentration of a specific compound in the surrounding medium decreases. The invention provides for means that prevent a significant dissolution of the coating or a significant detachment of the coating from the core(s) until the rinse cycles have begun. The invention also relates to a method for carrying out a wash cycle in a washing machine using the inventive composition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AI 19990729

SUMM Japanese patent KOKAI 50-77406 discloses a washing aid, which is

L57 ANSWER 11 OF 79 USPATFULL on STN (Continued)
surrounded by a water-soluble covering or envelope, obtained by mixing **polyvinyl** acetal diallyl aminoacetate and at least one organic acid, which is solid at room temperature. This protective envelope is intended.
DETD . . . silica, in order to give a free-flowing, granular material. The
resulting 0.25 g are mixed with 0.6 g of microcrystalline **cellulose** and 0.15 g of cross-linked **polyvinyl** pyrrolidone. The mixture is tabletted in a circular press with an internal diameter of 10 mm under a
pressure of. . . .
DETD 4 g of the granular composition were mixed with 1 g of **cellulose**. The mixture was tabletted in a circular press with an internal diameter of 25 mm and a pressure of 80. . . .
DETD . . . Sodium carbonate 7.43
Sodium LAS 40.0
Zeolite 17.70
Polymer 7.0
Sodium sulphate 9.61
Sodium-silicate 7.09
Soap 4.0
Phosphonate 1.55
Carboxymethyl **cellulose** 1.01
Water and others 4.7
DETD
TABLE 3

Ingredient wt. %

Spray-dried basic material 22.6
Sodium percarbonate 20.0
Sodium carbonate 29.18
Sodium tripolyphosphate 17.42
Microcrystalline **cellulose** 6.0
Alkyl sulphate 6.0
Polymer 1.50
Cross-linked **polyvinyl** pyrrolidone 1.80
Enzymes 1.78
TAED 3.00
Polyethylene glycol 0.18
Water and others 2.14
DETD . . . in the ionic concentration, i.e. Ionic concentration-sensitive polymers. Consideration for this purpose can e.g. be given to the partly
hydrolyzed **polyvinyl** acetates (commercially available under the trade mark Mowiol®--Clariant) described in EP 284 191 A2 and EP 284 334 A2 and. . . .
DETD . . . provided with a covering in an apparatus for the application of
a film coating, such as is known from the **pharmaceutical** industry (e.g. from Ledige, Ruttlo, GB, Moiesty ant Bruan).
DETD . . . provided with a protective coating. For this purpose use can be

L57 ANSWER 11 OF 79 USPATFULL on STN (Continued)
(Shells), detergent tablets for use in washing machines)

L57 ANSWER 12 OF 79 USPATFULL on STN (Continued)
made of various prior art materials such as e.g. **cellulose, cellulose** derivatives, **polyvinyl** alcohol, **polyvinyl** alcohol derivatives and mixtures thereof. When using the mass of example 1, in cases la, lb and lc such a protective coating was used, namely a 10
wt.% . . .
aqueous solution of the **polyvinyl** alcohol Mowiol® 5-88 (Clariant). In the case of example la the core was coated with 0.76 g of such a. . .
DETD . . . example 3 and 4 is introduced into the half-tablet recess. Subsequently a fixing substance e.g. an adhesive (e.g. polyethylene glycol, **polyvinyl** ether, **polyvinyl** alcohol, xiliate, preferably melted PEG 6000) is applied to the corresponding face of the half-tablet
and optionally also to the. . .
DETD
TABLE 4

Ingredient wt. %

Sodium carbonate 20
Trisodium citrate 20
Polymer 18.5
Schist silicate 10
Microcrystalline **cellulose** 10
Polyethylene glycol 6000 35
Phosphonate 3
Water 8.5
DETD
TABLE 5

First layer (26%) Second layer (74%)
Ingredient wt. % wt. %

Sodium percarbonate 75.93
Citric acid 17.50 8.10
Microcrystalline **cellulose** 7.00 7.00
Schist silicate 5.00 5.00
Enzymes 5.06
Sodium bicarbonate 9.94 1.37
TAED 50.00
Polyethylene glycol 6000 4.00 4.00
Polyvinyl pyrrolidone 1.50 1.50
Miscellaneous 0.068
IT **Polyvinyl** acetals
(dimethylamino)acetate esters, shells; detergent tablets for use in washing machines)
IT **9000-07-1,** Carrageenan 26322-40-2, Styrene-4-vinylpyridine copolymer 51391-20-92, acetal deriva. 182499-90-1, 2-(Dimethylamino)ethyl methacrylate-N-[3-(dimethylamino)propyl]methacrylamide-methyl methacrylate copolymer **(shells;** detergent tablets for use in washing machines)
IT **9000-07-1,** Carrageenan

L57 ANSWER 12 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2004:197271 USPATFULL
TITLE: Edible coating composition
INVENTOR(S): Aspelin, Michael, Marlboro, NJ, United States
Dell, Sheila M., New Hope, PA, United States
Tsarom, Domingo C., Bensalem, PA, United States
Modliszewski, James J., Brick, NJ, United States
Ruszkay, Thomas A., Hockessin, DE, United States
Werner, David E., West Grove, PA, United States
PATENT ASSIGNEE(S): FMC Corporation, Philadelphia, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6723342	B1	20040420	
APPLICATION INFO.:	US 2000-632228		20000804 (9)	<--
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2000-491724, filed on 27 Jan 2000, now patented, Pat. No. US 6432448			

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-172526P	19991217 (60)	<--
	US 1999-167607P	19991124 (60)	<--
	US 1999-162514P	19991028 (60)	<--
	US 1999-133992P	19990507 (60)	<--
	US 1999-119025P	19990208 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Speer, James M.
ASSISTANT EXAMINER: Di Nola-Baron, Lillian
LEGAL REPRESENTATIVE: Woodcock Washburn LLP
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 1602
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An edible, hardenable **coating** composition containing microcrystalline **cellulose** and **carrageenan** and at least one of a strengthening polymer, a plasticizer, a surface active agent or a combination thereof.
The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An edible, hardenable **coating** composition containing microcrystalline **cellulose** and **carrageenan** and at least one of a strengthening polymer, a plasticizer, a surface active agent or a combination thereof.
The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.
SUMM This invention relates to edible, hardenable, prompt **release coating**

L57 ANSWER 12 OF 79 USPATFULL on STN (Continued)
compositions comprising microcrystalline **cellulose** (MCC), **carrageenan** (CGN) and at least one of a strengthening polymer or a plasticizer. The coatings of the present invention can be applied to **pharmaceutical**, including nutriceutical, and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets
and granules, and foods, are readily. . . media, and, when applied as
a coating and ingested by, for example, a human, do not significantly retard or extend **release** of active ingredient(s) from a substrate coated therewith.

SUMM It is a common practice to coat **pharmaceutical** and veterinary tablets to obtain several advantages. Among these are to mask unpleasant tasting
active ingredients with a barrier coat.

SUMM Another very important function of a **pharmaceutical** or veterinary tablet coating is to improve the integrity of the tablet itself. Uncoated tablets are often subject to being.

SUMM Currently, most commercially available edible coatings utilize a synthetic **cellulosic** polymer such as **hydroxypropylmethylcellulose** (HPMC). Other synthetic film formers which are commonly used include **ethylcellulose**, **methylcellulose**, **polyvinylpyrrolidone**, and
polydextrose. These coating materials may be used alone or in combination with secondary film formers and various additives or. .
. . proportion to the increase in disintegration time. Many other admix commonly used in coating compositions are also known to delay **release** of **pharmaceutical** ingredients. For example, tablets which use polymeric film forming materials which are insoluble in water, or gastric fluid, some of these being specifically selected to by-pass both
the stomach and small intestine and provide colonic **release**.

SUMM The coatings of this invention meet U.S. **Pharmacopoeia** standards for rapid or immediate dissolution of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or disintegration of the coating and **release** rates which is normally obtained with the uncoated tablets or other substrates. Thus, they provide prompt **release** of the desired amount of active ingredients from a substrate coated with them. Further, the coatings of this invention meet the readily disperse standard, i.e.
. . . with the present invention by a coating composition which comprises a unique combination of materials specifically adapted for a prompt **release** when placed aqueous media or ingested, e.g., by a human. The coating composition of the present invention comprises microcrystalline **cellulose**, carrageenan, and at least one of a strengthening polymer and a plasticizer. More specifically, the present invention provides a prompt **release**, edible, hardenable coating composition comprising 78 to 40% microcrystalline **cellulose**, 98 to 20% **carrageenan**, and at least one of a strengthening polymer, a plasticizer, or a surface active agent, as well as dye.

SUMM The present invention also provides **pharmaceutical**, including nutriceutical, and veterinary solid dosage forms, confectionery, seeds,
animal feed, fertilizers, pesticide tablets and granules, and foods

L57 ANSWER 12 OF 79 USPATFULL on STN (Continued)
about 1-5 minutes, the wall valve is opened rapidly, **releasing** the contents explosively and yielding microcrystalline **cellulose**. No additional acid need be introduced to be near the optimum, since it is believed that the acidic materials in the wood chips and the elevated
temperature and pressure hydrolyze the **cellulose** and degrade it. In addition to the specific microcrystalline cellulose products that the present invention also contemplates the use of other **cellulose** derivatives, including regenerated cellulose. The term known as microcrystalline cellulose **cellulose**, and powdered **cellulose** such as a commercial material sold by Solka Floc® Division and in greater detail below, the microcrystalline **cellulose** preferred for use in the present invention is microcrystalline cellulose having an average particle size below about 100 microns, preferably microcrystalline **cellulose** having a mean or bulk average particle size in the range of 1 to 50 microns, preferably 1 to. . . Carrageenan is used in combination with microcrystalline **cellulose** to form the elegant prompt **release coatings** of the present invention. **Carrageenan** for use in the present invention is a partially derived carrageenan, including the grades further defined below as iota, kappa,
. . . sulfate content of iota carrageenan may range from about 25% to 34%, preferably about 32%. Typical sulfate content of iota **carrageenan** which has a **25%** ester sulfate content and lambda carrageenan which has a 38% ester sulfate content. The gelation salt of iota carrageenan is. . . Iota carrageenan require heating water to different temperatures to dissolve. The iota carrageenan which are
suitable for the microcrystalline **cellulose**/iota carrageenan material of this invention are soluble in water heated up to 80° C. (176° F.). Preferred grades of iota carrageenan

SUMM The microcrystalline **cellulose** and carrageenan may be coprocessed or may be blended in any suitable manner, such as dry blending.

SUMM Coprocessed microcrystalline **cellulose**/iota carrageenan is rapidly peptizable. Peptization means that the dry agent can readily be dispersed in water in a manner that. . . be dispersed (peptized)
in a colloidal state with minimal agitation. Thus, the novel coating formulations in which the coprocessed microcrystalline **cellulose**/iota carrageenan is incorporated can be hydrated in as little as 0.5 hour, but more preferably require 1 to 3 hours. . . .

SUMM The coprocessed microcrystalline/iota carrageenan compositions useful in
this invention may be prepared by first stirring hydrolyzed **cellulose** wetcake, such that the average particle size of the wetcake particles is
. . . generally not more than about 20 microns, preferably. . . at which the particular grade of iota carrageenan being used dissolves, adding the dry carrageenan to the dispersion of microcrystalline **cellulose**, mixing the components, preferably homogenizing the mixture to assure intimate mixing, and drying the dispersion. Spray-drying is normally used to. . . .

SUMM . . . is possible to prepare the coatings directly, that is, before the drying of the wetcake, from a dispersion of microcrystalline **cellulose** wetcake and the carrageenan by accounting for the water present in the wetcake and adding the other ingredients in the. . . coats for a dispersion would be less economical. Furthermore, drying by any method may enhance the association of the microcrystalline

L57 ANSWER 12 OF 79 USPATFULL on STN (Continued)
coated with the prompt **release**, edible, hardenable composition of this invention.

SUMM . . . application, the term 'edible' is intended to mean food grade materials which are approved by regulatory authorities for use in **pharmaceutical** or food applications. The term "hardenable" used to describe the coating compositions of this invention is intended to include only. . . that can be handled and packaged but which do not resist abrasive forces significantly. The terms "immediate", "rapid" or "prompt" **release** as applied to dissolution rates or times for the coating compositions of this invention or tablets coated with the compositions of this invention means that the coatings of this invention
meet U.S. **Pharmacopoeia** standards (U.S.P. monograph 23) for rapid or immediate dissolution of active ingredients from tablets or other solid dosage forms coated therewith. Thus, they provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrate. They do not, consistent with the **pharmacopoeia** standards above, when placed in aqueous media or ingested by, e.g., a human, significantly impact or retard **release** or dissolution of tablets or other solid dosage forms coated therewith. For example, coatings made in accordance with the present. . . completely disintegrated and/or dissolved within less than 10 minutes after being ingested or placed in aqueous media. Thus, when a **pharmaceutical** solid dosage form is coated with the coating of this invention and ingested by a human or other animal, the. . . .

SUMM The microcrystalline **cellulose**, either coprocessed with carrageenan or simply blended therewith, interacts with the carrageenan to provide important film-forming characteristics required to provide an elegant coating which is particularly useful in, for example, coating **pharmaceutical** and veterinary tablets, caplets, granules, and spheres which contain active ingredients which require **release** promptly after being placed in aqueous media or ingested.

SUMM Microcrystalline **cellulose** is a purified, partially depolymerized **cellulose** that is generally produced by treating alpha-type **cellulose**, preferably alpha **cellulose** in the form of a pulp from fibrous plants, with a mineral acid, preferably hydrochloric acid. The acid selectively attacks the less ordered regions of the **cellulose** polymer chain, thereby exposing and freeing the crystallites. Therefore, forming the crystallite aggregates which constitute microcrystalline **cellulose**. These are then purified by filtration of the aqueous acid washed to remove degraded by-products. The resulting wet mass, generally
containing 40 to 60 percent moisture, is referred to in the art by several names, including hydrolyzed **cellulose**, microcrystalline **cellulose**, microcrystalline **cellulose** wetcake, or simply wetcake. This microcrystalline **cellulose** wetcake may be used as such or may be further modified, for example, by attrition and/or drying, and utilized in.

SUMM Microcrystalline **cellulose** may also be produced for use in the present invention using a steam explosion treatment in which wood chips
or other **cellulosic** materials are placed in a chamber into which super-heated steam is introduced. After being maintained for a period
of

L57 ANSWER 12 OF 79 USPATFULL on STN (Continued)
cellulose with the carrageenan, which may result in a more satisfactory prompt **release** coating.

SUMM Dry blended microcrystalline **cellulose** (e.g., Avicel® PH-105, average particle size **20** microns) and iota **carrageenan**, has been found to provide **coating** compositions that can be applied to, and in some cases, superior to, coating compositions prepared from coprocessed microcrystalline **cellulose**/iota carrageenan.

SUMM . . . thereof is spread on a surface and allowed to dry. However, the
film is considered to be too weak for **pharmaceutical** tablets as shown by the results in Comparative Example A and therefore required the presence of microcrystalline **cellulose** for satisfactory results. A dry, physical blend of carrageenan and microcrystalline **cellulose** (Avicel® PH-102, average particle size 100 microns) also yielded what appeared to be unsatisfactory results as Comparative Example B. Thus, for commercial purposes, it is believed that the average particle size of microcrystalline **cellulose** used in a dry blend with the natural, film forming hydrocolloid should be below 100 microns, advantageously below about 50. . . . For performance coating formulations within the scope of this invention may be prepared from such dry, physical blends of microcrystalline **cellulose** and carrageenan.

SUMM A wide range of weight ratios of microcrystalline **cellulose** to **carrageenan** of from **90**:10 to about 15:85 may be employed in this invention. In those applications which require a higher ratio microcrystalline **cellulose** to carrageenan in the MCC+CGN weight ratio generally ranging from about 80:10 to about 60:40, typically from about 85:15 to. . . more particularly, approximately 70:30. In certain embodiments of this invention it has been found that relatively lesser amounts of microcrystalline **cellulose** can be employed, such that the ratio of MCC:CGN can be in the range of from about 15:85 up to. . . different ratios of coprocessed material. Thus, the dry, physical blends provide significantly greater flexibility for specific applications having different requirements. **Pharmaceutical** and veterinary solid dosage forms containing active ingredients may require increased carrageenan content in the composition to ideally coat
the tablets. For those **pharmaceutical** and veterinary applications, a preferred weight ratio of microcrystalline **cellulose** to carrageenan is in the range of about 75:25 to about 25:75.

SUMM Regardless of whether the coatings are based on coprocessed microcrystalline **cellulose**/carrageenan or a dry, physical blend of microcrystalline **cellulose** and carrageenan, a strengthening polymer, preferably, **hydroxyethylcellulose** (HEC) or **polyvinylpyrrolidone** (PVP), a plasticizer or both a strengthening polymer and a plasticizer and/or a surface active agent may be present in. . . Other strengthening polymers which can provide the same benefit and may be used instead of HEC include HPMC, **hydroxypropylcellulose**, **ethylcellulose**, and **methylcellulose**; however, care must be exercised in the use of such alternative materials to avoid significantly retarding **release** of active ingredients and/or bioavailability. The preferred amount of strengthening polymer is less than the total amount of microcrystalline **cellulose** and carrageenan present in the composition. Depending on the desired hardness of the coating, the strengthening polymer may be employed. . . . polymer is included in the
formulation. Strengthening polymers suitable for use in this invention

L57 ANSWER 12 OF 79 USPATFULL on STN (Continued)
and which will not significantly restrict **release** from tablets or other solid dosage forms, are those polymers having a viscosity equal to or less than 20 mPa.multidot.s.

SUMM The prompt **release** coating compositions of the invention may include at least one filler. Such fillers may include, for example, calcium carbonate, dicalcium.

SUMM The prompt **release** coating compositions of the invention may include at least one surfactant. Such surfactants include either anionic or nonionic surfactants. Useful.

SUMM . . . Basis a preferred composition of this invention comprises at least about 41%, suitably about 65% to about 75% of microcrystalline **cellulose** and carrageenan, in admixture combined, more preferably about 65% to about 69%; about 0.5% to about 30% of strengthening polymer, more.

. . .

SUMM . . . be specifically mentioned as being of special interest to this invention, in which there is provided an edible, hardenable, prompt **release** coating composition comprising about 7% to 65% microcrystalline **cellulose** in combination with about 9% to about 25% iota **carrageenan** and at least one of a strengthening polymer, a plasticizer, or a surface active agent, wherein said coating composition

is rapidly hydratable and does not, when ingested or placed in an aqueous medium, significantly retard the release of the ingredients from a substrate to which said coating is applied. Any of the strengthening polymers, plasticizers, surface active.

SUMM For example, a first of these embodiments comprises an edible, hardenable, prompt **release** coating composition comprising about 5% to about 25%, more particularly about 5% to 10%, microcrystalline **cellulose**; about 10% to about 16%, more specifically about **14%** to **16%**, iota **carrageenan**. Such embodiments may also contain about 2% to about 20% of a surface active agent such as lecithin, about 5% to about 70% propylene glycol alginate. These compositions may also contain 5% to 20% of a strengthening polymer such as

polyvinylpyrrolidone or **hydroxythicellulose**. A mixture of strengthening polymers such as the two aforesaid may also be employed. In addition, from about 2% to . . . filler such as maltodextrin, dicalcium phosphate, microcrystalline cellulose and a plasticizer may be employed. In this embodiment a reduced level of microcrystalline **cellulose** may be employed together with a small amount of processing agents such as a high level of lactose used as the filler. Such a particular composition may comprise 5% to 10% microcrystalline **cellulose**, 14% to 16% iota **carrageenan**, 2% to 4% hydroxylated soy lecithin, 65% to 70% lactose, and may include from about 5% to about 30% propylene glycol . . . range of about 15:85 up to 60:40, or more particularly 15:85 to about 50:50; and the combined total of microcrystalline **cellulose** and **carrageenan** comprises from about 20% to about 40% of the coating composition. When PVP is used as the sole strengthening polymer, it is preferably employed.

SUMM . . . the coating composition of this invention comprises about 30% to about 40%, in particular about 33% to about 38%, microcrystalline **cellulose**; about 10% to about 20%, more specifically about 14% to about **17%**, iota **carrageenan**, and about **12%** to about 25%, more specifically about 12% to about 22% of a strengthening polymer such as

L57 ANSWER 12 OF 79 USPATFULL on STN (Continued)
from the known drawbacks of HPMC.

SUMM All components of the formulation are typically **pharmaceutically** acceptable, edible food grade materials.

DETD In a Patterson-Kelley twin shell blender were placed 14.43 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), **18.36** grams of **polyvinylpyrrolidone** 29/32 (GAF), 16.40 grams of polyethylene glycol 8000, 0.30 grams of yellow #5 dye, and 0.2 grams of yellow #1 food color. After.

DETD By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), **0.25** gram of **hydroxythicellulose** (Aqualon® 250 L, Hercules Incorporated), 10.40 grams of polyethylene glycol 8000, and 0.30 gram

of yellow #5 food color was . . .

DETD By the method of Example 1, a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), **0.25** gram of **hydroxythicellulose** (Aqualon® 250 L, Hercules Incorporated), 5.40 grams of Maltrin® M-040 (Grain Processing Corporation), 5.40 grams of Maltrin® M-100, and 0.30 gram of Micro Talc, and 0.30 gram of.

DETD By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), **0.25** gram of **hydroxyethylcellulose** (Natrosol® 250 L, Hercules Incorporated), 10.40 grams of polyethylene glycol 8000, and 0.30 gram

of yellow #5 food color was . . .

DETD By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), **0.25** gram of **hydroxypropylcellulose** (Klucel® EF, Hercules Incorporated), 10.40 grams of polyethylene glycol 8000, 0.30 gram of yellow #1 food color, and 0.2 gram of vanillin was prepared. The resulting solution was sprayed using a Vector High Coater LDCS onto 1 Kg of cores comprised of 20% microcrystalline **cellulose** and 80% sugar (sucrose), each weighing on average 1.05 grams. Conditions used include an inlet temperature of 73-80° C., an.

DETD By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 10.65 grams of polyethylene glycol 8000, and 0.30 gram of yellow #5 food color was added to 400 grams of deionized . . . stirred while it was sprayed using a Vernier High Coater LDCS onto 1 Kg of the same cores of microcrystalline **cellulose** and calcium carbonate that were coated in Sample 5. Conditions used include an inlet temperature of 78-79° C., an outlet. . . in purified water at 37° C. . . . was less than 5 minutes. This coating was not as elegant as coatings containing **hydroxyethylcellulose**.

DETD By the method of Example 1 a dry mixture of 20.95 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 0.55 gram of **hydroxyethylcellulose** 250L, 11.40 grams of polyethylene glycol 8000, and 0.20 gram of yellow iron oxide was added to 450 grams of . . . solution was continuously stirred while it was sprayed using a Vector

High Coater LDCS onto 1.03 Kg of compressed microcrystalline **cellulose** cores (Avicel® PH-200) debossed with an FMC logo, each weighing on average 0.267 gram. Conditions used include an inlet temperature. . .

DETD By the method of Example 1 a dry mixture of 285.75 grams of spray-dried,
coprocessed microcrystalline **cellulose**/iota **carrageenan** (90:10), 7.5 grams of **hydroxyethylcellulose** 250L, 154.8 grams of polethylene

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hydroxypropylcellulose. These compositions may also further comprise about 5% to about 10%, more particularly 7% to 30%, of a surface active.

. . .

SUMM . . . third embodiment of the composition of this invention comprises

20% to 65%, more specifically about 33% to about 38% microcrystalline **cellulose**, 10% to 20%, more specifically about 15% to about **16%**, iota **carrageenan**, about **10%** to about 15% of a strengthening polymer such as **polyvinylpyrrolidone**, and 30% to 60%, more specifically 33% to 36%, of a plasticizer such as polyethylene glycol. This embodiment may further: . . . may be preferable to maintain agitation of the aqueous dispersion during the entire period of its storage to avoid the **pharmaceutical** or veterinary solid dosage form, confectionery, seeds, animal feed, fertilizer, pesticide tablets, or food.

SUMM The preferred edible, hardenable, prompt **release** coating formulations of this invention may generally be prepared and used according to a simple procedure. A dry mixture of coprocessed microcrystalline **cellulose**/carrageenan powder or a dry blend of microcrystalline **cellulose** and carrageenan, and a strengthening polymer, such as **hydroxythicellulose**, polethylene glycol or other compatible plasticizer, optionally together with a solid filler such as maltodextrin, lactose, mannitol and the like, . . .

SUMM In the formulations of microcrystalline **cellulose** and iota carrageenan, a simple propeller mixer provides adequate agitation for rapid hydration. The period of hydration may be as. . . thixotropic behavior of a formulation which sets up during overnight storage. Unlike

coating formulations based primarily on hydroxyalkyl ethers of **cellulose**, for example, HPMC, constant stirring of the microcrystalline and carrageenan based formulations of this invention does not need to be continued. . . .

SUMM . . . Engineering factors such as variables which one skilled in the art can manipulate to provide an elegant coating based on the microcrystalline **cellulose**/iota carrageenan blend, either coprocessed or dry blended, include inlet temperature, outlet temperature, air flow, speed of rotation of the . . .

SUMM **Hydroxythicellulose** binds water more effectively than carrageenan does. Thus, the presence of **HTC** in the formulations of carrageenan in the formulations of the carrageenan which dilutes the negative effects of HTC on drying time. Thus, in the case of incorporative **pharmaceutical** agents, for example, ibuprofen, the outlet temperature can be reduced and still provide short enough drying time to be commercially.

SUMM **Hydroxypropylcellulose** is particularly susceptible to clogging spray nozzles at high temperatures. An additional benefit provided by the formulations of this invention.

SUMM The level of coating applied to **pharmaceutical** or veterinary dosage forms is preferably between about 2% to about 5% by weight of the uncoated dosage form, more. . . to those of the uncoated tablets used as a substrate for coating. This is an additional unexpected benefit of the **coatings** based on **carrageenan** and microcrystalline **cellulose**, and it differs

L57 ANSWER 12 OF 79 USPATFULL on STN (Continued)
glycol 8000, and 65.0 grams of hydrolyzed red iron oxide was prepared. A portion (60. . . . have as elegant an appearance as those prepared in

Examples 1 through 7 in which the 70:30 combination of microcrystalline **cellulose** and iota carrageenan was used. Flaking or cracking was satisfactory, but there was minor chipping and erosion observed for these coated.

DETD By the method of Example 1 a dry mixture of 190.8 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota carrageenan (70:30), 5.02 grams of **hydroxyethylcellulose** 250L, 104.2 grams of polyethylene glycol 8000, 1.65 grams of methyl paraben, 0.165 gram of propyl paraben, 18.48 grams of.

DETD By the method of Example 1 a dry mixture of 194.7 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota carrageenan (70:30), 5.61 grams of **hydroxyethylcellulose** 250L, 106.4 grams of polyethylene glycol 8000, 1.65 grams of methyl paraben, 0.165 gram of propyl paraben, 18.48 grams of.

DETD By the method of Example 1 a dry mixture of 68.94 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 1.83 grams of **hydroxyethylcellulose** 250L, 37.62 grams of polyethylene glycol 8000, 0.545 grams of methyl paraben, 0.0545 gram of propyl paraben, 18.24 grams of.

DETD In a Patterson-Kelley twin shell blender were placed 229.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 160.65 grams) and iota carrageenan (68.85 grams), 49.5 grams of **hydroxyethylcellulose** (Natrosol® 250L), 148.5 grams of polyethylene glycol 8000 (Union Carbide Corporation), 13.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation).

DETD By the method of Example 12, a dry blend comprising 238.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 166.95 grams) and iota carrageenan (71.55 grams), 40.5 grams of **hydroxyethylcellulose** (Natrosol® 250L), 148.5 grams of polyethylene glycol 8000 (Union Carbide Corporation), 13.5 grams of maltodextrin (Maltrin® M-180), and 27.0 grams of FD&C Blue #1 Lake, 50 mL 0.05 M phosphate buffer at 36 minutes showed that 100% of the acetaminophen had been **released** at pH 5.8 and 97% of the ibuprofen had been **released** at pH 7.2. Dissolution testing using USP apparatus 1 (basket) at 50 rpm, 500 mL 0.05 M acetate buffer, pH 4.5 showed that 93&l.0% of the aspirin had been **released**.

DETD By the method of Example 12, a dry blend comprising 238.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 166.95 grams) and iota carrageenan (71.55 grams), 40.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 148.5 grams of polyethylene glycol 8000 (Union Carbide Corporation), and 22.5 grams of maltodextrin (Maltrin® M-180), was dispensed. . . 96° C hydration required 75 minutes. A Accela-Cota coater was charged with 12 Kg of cores comprised of 20% microcrystalline **cellulose** and 80% calcium carbonate, each weighing on average 1.05 grams. The coater was operated at an inlet

temperature of 92.8-100.3°.

DETD In a Patterson-Kelley twin shell blender were placed 234.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 164.5 grams) and iota carrageenan (67.5 grams), 67.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 63.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), 67.0 grams of titanium dioxide, and 22.5 grams of. . . .

DETD In a Patterson-Kelley twin shell blender were placed 76.5 grams of a

L57 ANSWER 12 OF 79 USPATFULL on STN (Continued)
blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**21**.0 grams), **22**.5 grams of **hydroxyethylcellulose** (Natrosol® 250L), 31.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), 10.0 grams of Red #40 aluminum lake, and 0.5 . . .
DETD In a Patterson-Kelley twin shell blender were placed 78.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**21**.0 grams), **22**.5 grams of **hydroxyethylcellulose** (Natrosol® 250L), 28.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), 10.0 grams of a red dye blend (Warner Jenkinson), . . .
DETD In a large Patterson-Kelley twin shell blender were placed 1.940 Kg of a
blend of microcrystalline **cellulose** (Avicel® PH-102, 1.358 Kg) and iota carrageenan (0.582 Kg), 0.436 Kg of **hydroxyethylcellulose** (Aqualon® 250L), 0.291 Kg of maltodextrin (Maltrin® M-180, Grain Processing Corporation), and 1.307 Kg of polyethylene glycol 8000 (Union
Carbide. . .
DETD In a Patterson-Kelley twin shell blender were placed 72.80 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 50 .**25** grams) and iota **carrageenan** (**14**.55 grams), 35.00 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 44.15 grams of hydrophilic red iron oxide. After being thoroughly mixed, the dry components were added to . . .
DETD In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**18**.0 grams), 23.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), 33.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), and 22.5 grams of hydrophilic yellow oxide. After being. . .
DETD In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**18**.0 grams), 23.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 22.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation). Simultaneously 22.5 grams of titanium dioxide was added. . .
DETD In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**18**.0 grams), 23.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 12.0 grams of maltodextrin (Maltrin M-280, Grain Processing Corporation). Simultaneously 31.5 grams of titanium dioxide was added. . .
DETD In a Patterson-Kelley twin shell blender were placed 78.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**22**.5 grams), 9.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 9.0 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation). Simultaneously 30.0 grams of titanium dioxide was added. . .
DETD In a Patterson-Kelley twin shell blender were placed 73.25 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 49.94 grams) and iota **carrageenan** (**21**.39 grams), **14**.01 grams of **hydroxyethylcellulose** (Aqualon® 250L), 48.05 grams of polyethylene glycol 8000 (Union Carbide Corporation), 10.19 grams of maltodextrin

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(Maltrin M-180, Grain Processing Corporation). . .
DETD In a Patterson-Kelley twin shell blender were placed 78.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**22**.5 grams), 93.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 1.5 gram of stearic acid. Simultaneously 97.5 grams of titanium dioxide was added to 1516.7 grams of . . .
DETD In a Patterson-Kelley twin shell blender were placed 780 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, **200** grams) and iota **carrageenan** (**100** grams), and **100** grams of polyethylene glycol 8000 (Union Carbide Corporation). After the dry components had been thoroughly blended, the entire blend was . . .
DETD In a Patterson-Kelley twin shell blender were placed 49.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 74.5 grams) and iota **carrageenan** (**14**.7 grams), **11**.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), 73.0 grams of polyethylene glycol 8000 (Union Carbide Corporation), 7.0 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation), . . .
DETD In a Patterson-Kelley twin shell blender were placed 67.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 73 grams) and iota **carrageenan** (**10** grams), **20** grams of **hydroxyethylcellulose** (Aqualon® 250L), 23.0 trans of triacetin, 4.0 grams of propylene glycol alginate, and 3 grams of Pluronic F-68 (BASF). After. . .
DETD

Amount
Ingredient (g)

Microcrystalline **cellulose** 37.5
(Avicel PH-**105**)
Iota **carrageenan** **14**.7
Polyethylene glycol 8000 34
Hydroxyethylcellulose 250L 11
Maltodextrin M-180 9
DETD

Example:
31 22 03
Weight (grams)

Avicel PH-105 55 34.3 34.3
Iota **carrageenan** **11** **14**.7 **14**.7
Hydroxyethylcellulose -- 11 11
PGA.sup.a 7 . .
PEG.sup.b 34 33 33
Lecithin.sup.c 7 4 7
Maltrin M-180 3 3

.sup.aPropylene glycol alginate (Protonal ® ester SD-LB, Pronova). . . .
DETD

Weight
(grams)

L57 ANSWER 12 OF 79 USPATFULL on STN (Continued)
Avicel PH-**105** 33
Iota **carrageenan** **14**.5
Hydroxyethylcellulose **22**
Mannitol,sp.g. 15.5
Pluronic F-68 3
Blue Lake #2 8
Deionized water 1150
Hydration time 2.5
Caplets
Imugreen 1 kg
Anetaminophen. . .
DETD
TABLE 1

Example: 36 37 38 39 40 41 42 43 44 45 46 47

Ingredients
Microcrystalline **cellulose** 5 7 9 9 9 9 9 10 10 12.3 **13** 15
Iota **Carrageenan** **15** **15** **14** 14 14.5 14.5 15 10 14 14.7 14 14
Polyvinylpyrrolidone 24 12 14 .sup. 7 14 .sup.a 14 10 14 14 14 10 5 5
Hydroxyethylcellulose
Lecithin.sup.@ 2 2 2.5 3 2 2.5 2 2 2 2 2 2 2
Lactose 60 60 60 60 60 64 60 60 62. . . 100 100 100 100 100 100 100 100 100

Example: 48 49 50 51 52 53 54 55 56 57 58

Ingredients
Microcrystalline **cellulose** 15 19 20 20 25 7 23 35 34.3 33-36 37.3
Iota **Carrageenan** 14 14.5 15 10 15 16 17 18 14.7 15-17 14.7
Polyvinylpyrrolidone 7.5 7.5 14 . . . 11
Hydroxyethylcellulose 20 22 22 22 22 13 22
Lecithin.sup.@ 3 3 5 7 8 3 10 7 8-10
Lactose 40 40 35 47. . .
DETD A dispersion of 8.2G grams of microcrystalline **cellulose** (Avicel® PH-202, FMC Corporation) and 20.7 grams of iota carrageenan (Viscarin® SD-389) in 1300 grams of deionized water was prepared. .

CLM What is claimed is:
1. An edible, hardenable, prompt **release pharmaceutical** or veterinary solid dosage form coating composition comprising 3% to 40% microcrystalline **cellulose** having an average particle size less than 100 microns, a film forming amount of carrageenan, and at least one of a
strengthening polymer, a plasticiser, or a surface active agent,
wherein

L57 ANSWER 12 OF 79 USPATFULL on STN (Continued)
said **pharmaceutical** or veterinary solid dosage form coating composition does not, when ingested or placed in an aqueous medium, significantly retard **release** of active ingredients from a solid dosage form to which said coating is applied and said film forming amount of **carrageenan** is 9% to **25**%.

CLM What is claimed is:
2. The coating composition of claim 1 comprising 5% to 25% microcrystalline **cellulose**, 10% to **14**% iota **carrageenan**, and **2**% to **10**% hydroxylated soy lecithin.

CLM What is claimed is:
5. The coating composition of claim 2 comprising 5% to 22% of **hydroxyethylcellulose**, or **polyvinylpyrrolidone**.

CLM What is claimed is:
7. The coating composition of **claim** 1 comprising 5% to 10% microcrystalline **cellulose**, **14**% to **16**% iota **carrageenan**, **2**% to 4% hydroxylated soy lecithin, 65% to 70% lactose and 5% to 10% propylene
glycol alginate.

CLM What is claimed is:
9. The coating composition of claim 1 comprising 30% to 40% microcrystalline **cellulose**, **10**% to **20**% iota **carrageenan**; and **12**%-**25**% **hydroxyethylcellulose**.

CLM What is claimed is:
13. The coating composition of claim 1, comprising 30% to 40% microcrystalline **cellulose**, **10**% to **20**% iota **carrageenan**, 10% to **15**% **polyvinylpyrrolidone**, and 30% to 40% polyethylene glycol.

CLM What is claimed is:
. . . coating composition of claim 1, wherein said strengthening polymer is
at least one member selected from the group consisting of **hydroxypropylcellulose**, **hydroxypropylmethylcellulose**, **hydroxypropoylmethylcellulose** and **polyvinylpyrrolidone**.

CLM What is claimed is:
19. An edible, hardenable, prompt **release pharmaceutical** or veterinary coating composition comprising 3% to 40% microcrystalline **cellulose**, a film forming amount of carrageenan, and at least one of a strengthening polymer, a plasticizer, or a surface active agent,
wherein
said **pharmaceutical** or veterinary solid dosage form coating composition does not, when ingested or placed in an aqueous medium, significantly retard **release** of active ingredients from a solid dosage form to which said coating is applied and said film forming amount of **carrageenan** is 9% to **25**%.

CLM What is claimed is:
20. A method for coating a **pharmaceutical** or veterinary solid dosage form comprising the steps of hydrating the coating composition of claim 1, followed by spray coating said hydrated coating composition onto
said
pharmaceutical or veterinary solid dosage form.

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CLM What is claimed is:
22. A **pharmaceutical** or veterinary solid dosage form coated with the coating composition of claim 1.

CLM What is claimed is:
24. A **pharmaceutical** or veterinary solid dosage form coated with the coating composition of claim 19.

CLM What is claimed is:
25. The **pharmaceutical** or veterinary solid dosage form of claim 22, wherein said **pharmaceutical** solid dosage form is a nutraceutical solid dosage form.

CLM What is claimed is:
26. The **pharmaceutical** or veterinary solid dosage form of claim 22, wherein said coating composition further comprises a carbohydrate filler.

CLM What is claimed is:
27. The **pharmaceutical** or veterinary solid dosage form of claim 22, comprising 5% to 25% microcrystalline **cellulose**, 2% to 10% hydrogylated soy lecithin and 75% to 80% lactose.

CLM What is claimed is:
28. The **pharmaceutical** or veterinary solid dosage form of claim 22, wherein said **pharmaceutical** or veterinary solid dosage form is a tablet.

CLM What is claimed is:
29. The **pharmaceutical** or veterinary solid dosage form of claim 22, wherein said **pharmaceutical** or veterinary solid dosage form is a caplet.

IT Drug delivery systems
(caplets; edible coating compos. containing microcryst. **cellulose** and carrageenan)
IT Adhesion, physical
IT Coating materials
IT Dyes
IT Elongation, mechanical
IT Friability
IT Elasticizers
IT Stress, mechanical
IT Surfactants
IT Young's modulus
(edible coating compos. containing microcryst. **cellulose** and carrageenan)
IT Carbohydrates, biological studies
IT Polymers, biological studies
IT Polyoxyalkylenes, biological studies
(edible coating compos. containing microcryst. **cellulose** and carrageenan)
IT Drug delivery systems
(solids; edible coating compos. containing microcryst. **cellulose**

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ACCESSION NUMBER: 2004129201 USPATFULL
TITLE: Edible FGA coating composition
INVENTOR(S): Augello, Michael, Marlboro, NJ, UNITED STATES
Bliefernich, Eric, Yardville, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20040062855	A1	20040401
	US 6881409	B2	20050419
APPLICATION INFO.:	US 2003-654529	A1	20030903 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2001-994252, filed on 26 Nov 2001, PENDING		

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-284779P	20010419 (60)	<--
	US 2001-284609P	20010224 (60)	<--
	US 2000-253406P	20001128 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WOODCOCK WASHBURN LLP, ONE LIBERTY PLACE, 46TH FLOOR, 1650 MARKET STREET, PHILADELPHIA, PA, 19103
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
LINE COUNT: 609
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An edible, hardenable coating composition is disclosed which comprises high levels of low viscosity propylene glycol alginate and a surfactant, which may additionally contain a filler, a pigment, and optionally a small amount of a secondary film former and/or a strengthening polymer. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . of a secondary film former and/or a strengthening polymer. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

SUMM [0002] This invention relates to edible, hardenable prompt **release** coating compositions comprising a film forming amount of low viscosity propylene glycol alginate that serves as the principle, primary or sole film former of the coating composition. The coatings of the present invention can be applied to **pharmaceutical**, including nutraceutical, and veterinary solid dosage forms, such solid substrates such as seeds, animal feed, fertilizers, pesticide tablets and granules. . . . dispersed in aqueous media, and, when applied as a coating, provide high lustre coatings which do not retard or extend **release** of active ingredient from a coated substrate.

SUMM [0002] It is a common practice to coat **pharmaceutical** and veterinary tablets to obtain several advantages. Among these are to improve the

L57 ANSWER 12 OF 79 USPATFULL on STN (Continued)
and carrageenan)
IT Lecithins
(soya, hydrogenated; edible coating compns. containing microcryst. **cellulose** and carrageenan)
IT Diet
(supplements; edible coating compns. containing microcryst. **cellulose** and carrageenan)
IT Drug delivery systems
(tablets, coated; edible coating compns. containing microcryst. **cellulose** and carrageenan)
IT Drug delivery systems
(tablets; edible coating compns. containing microcryst **cellulose** and carrageenan)
IT 56-70-4, Sorbitol, biological studies 56-81-5, Glycerin, biological studies 57-55-6, Propylene glycol, biological studies 63-42-3, Lactose 77-92-9, Trisodium citrate 102-76-1, Triacetin 109-43-3, Dibutyl sebacate 151-21-3, Sodium lauryl sulfate, Biological studies **9000-07-1**, Carrageenan 9002-79-8, **Polyvinylpyrrolidone** 9004-62-0, Hydroxyethyl **cellulose** 9004-64-2, Hydroxypropyl **cellulose** 9004-65-3, Hydroxypropyl methyl **cellulose** 9005-37-2, Propylene glycol alginate 9050-36-6, Maltrin M-100 9062-07-1, κ-Carrageenan 25322-68-3, Polyethylene glycol 106392-12-5, Polyethylene glycol-polypropylene glycol block copolymer (edible **coating** compns. containing microcryst. **cellulose** and carrageenan)
IT 9004-34-6, **Cellulose**, biological studies
(microcryst.; edible coating compns. containing microcryst. **cellulose** and carrageenan)
IT **9000-07-1**, Carrageenan
(edible **coating** compns. containing microcryst. **cellulose** and carrageenan)

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surface characteristics of tablets to make them. . .
SUMM [0003] Another very important function of a **pharmaceutical** or veterinary tablet coating is to improve the integrity of the tablet itself. Uncoated tablets are often subject to being. . . . proportion to the increase in disintegration time. Many other agents commonly used in coating compositions are also known to delay **release** of **pharmaceutical** agents, such as enteric coatings which use polymeric film forming materials which are insoluble in water, or gastric fluids, some of these being specifically selected to by-pass both the stomach and intestine and provide colonic **release**.
SUMM [0011] The coatings of this invention meet U.S. **Pharmacopeia** standards for rapid or immediate dissolution (U.S.P. monograph 23) of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates. Thus, they do not adversely impact or retard **release** of active ingredients from a substrate coated with them. Further, the coatings of this invention are readily dispersed and rapidly . . . a secondary film former and/or a strengthening polymer as an additional ingredient. More specifically, the present invention provides a prompt **release**, edible, hardenable FGA coating composition, as well as dry coatings and aqueous dispersions thereof and solid dosage forms coated therewith.
SUMM [0013] For purposes of this application, the term "edible" is intended to mean food or **pharmaceutical** grade materials which are approved by regulatory authorities for use in **pharmaceutical** or food applications. The term "hardenable," used to describe the coating compositions of this invention, is intended to include only. . . this invention or tablets coated with the compositions of this invention, mean that the coatings of this invention meet U.S. **Pharmacopoeia** standards (U.S.P. monograph 23) for rapid or immediate dissolution of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates. They do not, when placed in water or ingested, adversely impact or retard **release** or dissolution of tablets or other dosage forms coated with them. Coatings made in accordance with the present invention are. . . .
SUMM . . . glycol alginate, provides important film-forming characteristics required to provide an elegant coating which is particularly useful in, for example, coating **pharmaceutical** and veterinary tablets, caplets, granules, and spheres which contain active ingredients which require **release** promptly after being placed in aqueous media or ingested. . . . may include a minor amount of secondary film former such as carrageenan or HPMC and/or a strengthening polymer such as **hydroxypropylcellulose**.
SUMM . . . example, calcium carbonate, dicalcium phosphate and carbohydrates, such as starch, maltodextrin, lactose, mannitol and other sugars, croscarmellose sodium, or microcrystalline **cellulose**. Of these, maltodextrin has been found beneficial at about 10% to about 30%

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by dry weight of the composition, but . . .
SUMM . . . formulation, it may be desirable to include a secondary film former such as carrageenan and/or a strengthening polymer such as **hydroxyethylcellulose**. While such additional additives are generally not required, they may be utilized if desired at about 3% to about 12%. . . .
SUMM . . . dry weight of the composition of a secondary film forming polymer such as carrageenan or a strengthening polymer such as **hydroxyethylcellulose**. Preservatives, such as methyl paraben at 0.75% to 2.50% and/or propyl paraben at 0.075% to 0.25% may also be present. . . .
SUMM . . . may be preferable to maintain agitation of the aqueous dispersion during the entire period of its being sprayed onto the **pharmaceutical** or veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizer, pesticide tablets, or food.
SUMM [0024] The preferred edible, hardenable, prompt **release** coating formulations of this invention may generally be prepared and used according to a simple procedure. Propylene glycol alginate and. . .
SUMM . . . thixotropic behavior of a formulation which sets up during overnight storage. Unlike coating formulations based primarily on hydroxyalkyl ethers of **cellulose**, for example, HPMC, constant stirring of the propylene glycol alginate-based formulations of this invention does not need to be continued. . . .
SUMM [0027] The level of coating applied to **pharmaceutical** or veterinary dosage forms is preferably between about 0.5% to about 4% by weight of the uncoated dosage form, more. . . .
SUMM [0031] All components of the formulation are typically **pharmaceutically** acceptable, edible food grade materials.
DETD . . . twin shell blender were placed 292 grams of low viscosity propylene glycol alginate (Profoam, Pronove/FMC Corporation) and 65 grams of **hydroxyethylcellulose** 250 L 22.5 grams of hydroxylated soy lecithin Frenagel 8310, Central Soya), 45 grams of maltodextrin M1 90 (Maltrin M1. . .

DETD . . .	55					
Lecithin.sup.2	3.3	5	7	5	2.5	5
Maltodextrin.sup.3	--	10	18	30	30	25
Pigment	13.4	10	10	--	7.5	10
SEC.sup.4	--	**10**	--	--	--	--
Iota **carrageenan**	--	--	--	--	--	5
Caplet Ingredients						
Acetaminophen					X	X
Ibuprofen	X	X	X			
Chlorpheniramine				X		
Coating Weight (4)	3	3	3	3	3	3
Friability. . . minutes				92	91	
60 minutes		99	99			

.sup.1Polypropylene glycol alginate (Profoam ®, Pronove/FMC Corporation)
.sup.2Hydroxylated soy lecithin, Central Soya
.sup.3Maltodextrin, Maltrin M180
.sup.4**Hydroxyethylcellulose** 250L
.sup.55 = excellent; 4 = acceptable; 3 = marginal; 2 = poor; 1 = Not acceptable

L57 ANSWER 14 OF 79 USPATFULL on STN (Continued)
carrageenan, latex polymers, and esteric **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.
DETD . . . Preferably, the outer coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVO-methylmethacrylate copolymer and PVP-PVA copolymer.
DETD [0038] Finally, a polymer coating solution was prepared by dissolving 6.35 kg of Elvanol 51-05 **polyvinyl** alcohol, 7.94 kg titanium dioxide and 1.59 kg Neodel 23-6.5T nonionic surfactant in 50.12 kg water and spraying over the. . .

L57 ANSWER 14 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2004139215 USPATFULL
TITLE: Granule with hydrated barrier material
INVENTOR(S): Becker, Nathaniel T., Burlingame, CA, UNITED STATES
Christensen, Robert I., Jr., Pinole, CA, UNITED STATES
Gaertner, Alfred L., San Bruno, CA, UNITED STATES
Ghani, Mahmood M., Milpitas, CA, UNITED STATES
Dale, Navojas A., Pacifica, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20040029756	A1	20040212
APPLICATION INFO.:	US 2003-630217	A1	20030730 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2000-581737, filed on 16 Jun 2000, GRANTED, Pat. No. US 6602841 A 371 of International Ser. No. WO 1998-US27214, filed on 21 Dec 1998, PENDING		

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1997-68382P	19971220 (60)	<--
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	JEFFERY D. FRASER, GENENCOR INTERNATIONAL, INC., 925 PAGE MILL ROAD, PALO ALTO, CA, 94304		

NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
LINE COUNT: 456
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A granule having high stability and low dust is described. The granule includes a hydrated barrier material having moderate or high water activity. Also described are methods of producing the granule.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . U.S. Pat. No. 4,106,991 describes an improved formation of enzyme granules by imbedding within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-40% w/w based on the dry weight of the whole composition. In addition, this patent. . . .
SUMM . . . Diatomaceous earth or sodium citrate crystals. The film forming material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.
SUMM . . . and improved stability formulations. Accomplishing all these desired characteristics simultaneously is a particularly challenging task since, for example, many delayed **release** or low-dust agents such as fibrous **cellulose** or waxy wire polymers learn behind insoluble residues.
DETD [0036] Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as enzymes
DETD [0028] Suitable coatings include **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose**, hydroxypropylmethyl **cellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan,

L57 ANSWER 15 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2003:302709 USPATFULL
TITLE: Hard capsule formed of **cellulose** ether film with a specific content of methoxyl and hydroxypropoxyl groups
INVENTOR(S): Nakayora, Setsuosuke, Kyoto, JAPAN
Taniyo, Masaru, Saitama, JAPAN
PATENT ASSIGNEE(S): Shionogi Qualicaps Co., Ltd., Yamatokoriyama, JAPAN (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6649180	B1	20031118
APPLICATION INFO.:	US 2000-549200	20000413 (9)	<--

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1999-104699	19990414 <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Peselnick, Paul	
ASSISTANT EXAMINER:	Bernatz, Kevin M.	
LEGAL REPRESENTATIVE:	Birch, Stewart, Kolasch & Birch, LLP	
NUMBER OF CLAIMS:	5	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	336	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A **cellulose** ether film is formed of a composition comprising a **cellulose** ether as a base in which some of the hydrogen atoms of **cellulosic** hydroxyl groups are replaced by alkyl groups and/or hydroxyalkyl groups, a gelling agent, and a gelling aid. The total content of alkoxyl and hydroxyalkoxyl groups in the **cellulose** ether is limited to 23-37.4% by weight, which is effective for preventing the gelling aid from precipitating out and maintaining a favorable outer appearance during long-term storage.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Hard capsule formed of **cellulose** ether film with a specific content of methoxyl and hydroxypropoxyl groups

AB A **cellulose** ether film is formed of a composition comprising a **cellulose** ether as a base in which some of the hydrogen atoms of **cellulosic** hydroxyl groups are replaced by alkyl groups and/or hydroxyalkyl groups, a gelling agent, and a gelling aid. The total content of alkoxyl and hydroxyalkoxyl groups in the **cellulose** ether is limited to 23-37.4% by weight, which is effective for preventing the gelling aid from precipitating out and maintaining.

SUM1 This invention relates to a **cellulose** ether film suited for use in forming pharmaceutical and food hard capsules.

SUM2 . . . to say type of film, the exemplary substitute for the gelatin capsules is capsules whose film is formed of a **cellulose** ether composition comprising a water-soluble **cellulose** ether as a base in

L57 ANSWER 15 OF 79 USPATFULL on STN (Continued)
which some of the hydrogen atoms of **cellulosic** hydroxyl groups are replaced by alkyl and hydroxyalkyl groups or hydroxyalkyl groups, a gelling agent, and a gelling aid, as disclosed in Japanese Patent No. 2,552,937. Some capsules based on hydroxypropoxyl methyl **cellulose** (HPMC) have been used in practice. These capsules of **cellulose** ether film maintain a sufficient strength even at a low water content, and their behaviors such as dissolution are equivalent.

SUM3 However, the capsules of **cellulose** ether film suffer from the problem that the gelling aid which is blended for assisting in film formation will precipitate . . .

SUM4 More particularly, in one appropriate formulation of the **cellulose** ether film for forming capsules, carrageenan is used as a gelling agent for HPMC, and a potassium or calcium ion . . . aid in the form of a water-soluble compound such as potassium chloride or calcium chloride. During long-term storage of these **cellulose** ether film capsules, the water content of the film can be changed by the surrounding environment or the water.

SUM5 An object of the invention is to provide a novel and improved **cellulose** ether film of a composition comprising a **cellulose** ether as a base, a gelling agent, and a gelling aid, which prevents the gelling aid from precipitating out and.

SUM6 It has been found that when a film, typically a capsule film is formed of a composition comprising a **cellulose** ether as a base in which some of the hydrogen atoms of **cellulosic** hydroxyl groups are replaced by alkyl groups and/or hydroxyalkyl groups, a gelling agent, and a gelling aid, the use of the **cellulose** ether having an alkoxyl and hydroxyalkoxyl content of up to 37.4% by weight is effective for preventing precipitation of the gelling aid.

SUM7 Accordingly, the invention provides a **cellulose** ether film formed of a composition comprising a **cellulose** ether as a base in which some of the hydrogen atoms of **cellulosic** hydroxyl groups are replaced by alkyl groups and/or hydroxyalkyl groups, a gelling agent, and a gelling aid, wherein the total content of alkoxyl and hydroxyalkoxyl groups in the **cellulose** ether is up to 37.4% by weight.

SUM8 . . . precipitation of the gelling aid can be restrained by limiting the total content of alkoxyl and hydroxyalkoxyl groups in the **cellulose** ether to 37.4% by weight or lower is not well understood, the following mechanism is inferred. As the **cellulose** ether used as the film base, some of the hydrogen atoms of **cellulosic** hydroxyl groups are replaced by alkyl groups and/or hydroxyalkyl groups whereby the hydroxyl groups are converted into alkoxyl or hydroxyalkoxyl. .

SUM9 Briefly stated, the **cellulose** ether film of the invention is manufactured by using a **cellulose** ether as a base, blending a gelling agent and a gelling aid therein, and forming the composition into a film.

SUM10 The **cellulose** ether used as the base is one in which some of the hydrogen atoms of **cellulosic** hydroxyl groups are replaced by alkyl groups and/or hydroxyalkyl groups whereby alkoxyl and/or hydroxyalkoxyl groups are created.

SUM11 Though not critical, the **cellulose** ether is preferably one in which some of the hydrogen atoms of **cellulosic** hydroxyl groups are replaced by alkyl groups and hydroxyalkyl groups or by hydroxyalkyl groups. Of the alkyl groups, methyl is preferred. Of the hydroxyalkyl groups, hydroxypropyl or hydroxyethyl is preferred. Illustrative

L57 ANSWER 15 OF 79 USPATFULL on STN (Continued)
examples of the **cellulose** ether substituted with these groups include hydroxypropyl methyl **cellulose** (HPMC), hydroxypropyl **cellulose** (HPC), hydroxyethyl methyl **cellulose** (HEMC), and hydroxyethyl **cellulose** (HEC). Of these, HPMC is best suited for capsule film application because

of effective film formation and mechanical strength at . . .

SUM12 According to the invention, the alkoxyl and hydroxyalkoxyl groups created in the **cellulose** ether by introducing the above substituents are limited to 23-37.4% by weight. More particularly, the total content corresponds . . . and hydroxyethoxyl groups in the case of HEC, and the sum of MO groups in the case of MC. A **cellulose** ether having a total content of such substituents of up to 37.4% by weight is used.

SUM13 Of the above-described **cellulose** ethers, HPMC, HPC, and MC are specified in the Pharmacopoeia of Japan. In the capsule shell application, it is recommended.

SUM14 For HPMC, the Pharmacopoeia specifies three types, hydroxypropoxyl methyl **cellulose** 2208, hydroxypropoxyl methyl **cellulose** 2906, and hydroxypropoxyl methyl **cellulose** 2910, depending on the contents of MO and HPO groups. It is specified that hydroxypropoxyl methyl **cellulose** 2208 contains 19 to 24 wt % of MO groups and 4 to 12 wt % of HPO groups in a total of 23 to 36 wt %; hydroxypropoxyl methyl **cellulose** 2906 contains 27 to 30 wt % of MO groups and 4 to 7.5 wt % of HPO groups in a

total of 31 to 37.5 wt %, and hydroxypropoxyl methyl **cellulose** 2910 contains 28 to 30 wt % of MO groups and 7 to 12 wt % of HPO groups in a total of 35 to 42 wt %. Of these, **cellulose** may be used in the practice of the invention as long as the total content of MO and HPO groups is up to 37.4 wt %. Also acceptable are those in which any two

or more of these **cellulose**s are mixed to adjust the total content of MO and HPO groups to that range.

It is noted that the sum of alkoxyl and hydroxyalkoxyl groups in **cellulose** ether can be determined by the measurement method described in the Pharmacopoeia for the HPMC, HPC and MC specified therein, and by a well-known method for the remaining **cellulose** ethers.

SUM15 The gelling agent used may be selected from among, for example, carrageenan, tamarind seed polysaccharide, gellan gum, furcellaran,

gellan gum, and mixtures thereof. Of these, carrageenan is especially preferred because it has a high gel strength and exhibits good gelling.

SUM16 . . . amount of the gelling agent used is not critical and may be suitably determined in accordance with the type of **cellulose** ether and gelling agent, the intended application of film, and film forming method. When capsule shells are formed by the . . . especially about 0.25 to 15 parts by weight of the gelling agent per 100 parts by weight of the **cellulose** ether. Less than 0.25 part of the gelling agent may achieve a lower degree of gelation and fail to produce. . .

SUM17 . . . ion, calcium ion, ammonium ion, and various organic compounds which can promote gelation by the gelling agent. Especially when capsule

shells are formed using **carrageenan** as the gelling agent, a potassium ion or calcium ion or both are preferably used. The potassium ion may be . . .

SUM18 . . . amount of the gelling aid used is not critical and may be suitably determined in accordance with the type of **cellulose** ether and gelling agent, the intended application of film, and film forming

L57 ANSWER 15 OF 79 USPATFULL on STN (Continued)
method. When capsule shells are formed by the . . . 0.25 to 15 parts by weight, calculated as ion, of the gelling aid per 100 parts by weight

of the **cellulose** ether. Less than 0.05 part of the gelling aid may promote gelation of the gelling agent to a less extent.

SUM19 While the **cellulose** ether film of the invention contains the **cellulose** ether as the base, the gelling agent and the gelling aid, there may be added appropriate amounts of various additives.

SUM20 The **cellulose** ether film of the invention is manufactured by well-known method depending on its application. When hard capsules are formed from the **cellulose** ether film of the invention, for example, the film can be prepared in the form of capsule shells by a well-known dipping method as

in the manufacture of conventional gelatin capsules. In one exemplary process, the **cellulose** ether, the gelling agent, gelling aid and optional additives are disolved in water in appropriate amounts as mentioned above to form . . . bodies of the outside surface of the pins whereupon the shells are removed from the pins. In this way, the **cellulose** ether film of the invention is obtained in the form of capsule shells. The shells are then cut to a predetermined size and mated to construct hard capsules of the **cellulose** ether film according to the invention.

SUM21 As mentioned above, the dipping solution is an aqueous solution having predetermined amounts of the **cellulose** ether, gelling agent, gelling aid and optional additives blended therein. This aqueous solution is preferably prepared to a concentration of 15 to 30% by weight, and especially 18 to 28% by weight of the **cellulose** ether. Less than 15% by weight of the **cellulose** ether may fail to form a film of a sufficient thickness to serve as capsule shells whereas more than 30%

by

weight of the **cellulose** ether may provide the dipping solution with too high a viscosity to form a uniform film. The remaining constituens may be the same as those customarily used in the manufacture of **cellulose** ether-based capsules.

SUM22 The **cellulose** ether film of the invention is suitable as the shell of hard capsules for use in the pharmaceutical and health.

DET3 Hydroxypropyl methyl **cellulose** 2910 specified in the Pharmacopoeia of Japan ("Metolose 60SH" by Shin-Etsu Chemical Co., Ltd.) and hydroxypropyl methyl **cellulose** 2208 ("Metolose 90SH" by Shin-Etsu Chemical Co., Ltd.) were mixed in the proportion shown in Table 1.

Using

this hydroxypropyl methyl **cellulose**, a dipping solution of the composition shown below was prepared. By a conventional dipping method, size No. 2 hard capsules of colorless clear hydroxypropyl methyl **cellulose** film of about 100 microns thick were prepared therefrom. Note that the contents of methoxyl and hydroxypropoxyl groups in hydroxypropyl methyl **cellulose** 2910 (Metolose 60SH) and hydroxypropyl methyl **cellulose** 2208 (Metolose 90SH) were determined by the measurement method prescribed in the Pharmacopoeia of Japan, with the results shown below.

DET5

Hydroxypropyl methyl **cellulose** 20 wt %
κ-carrageenan (gelling agent) 0.3 wt %
Potassium chloride (gelling aid) 0.1 wt %
10.652 wt % of.

DET6

TABLE 1

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Cellulose Precipitation of KCl
mixture of total content of or capsule surface
2910:2208 OCH3.sub.3 + OC.sub.3H.sub.6OH (40 °C., 1 month)
(weight)
DETD As seen from Table 1, controlling the total content of alkoxyl and
hydroxyalkoxyl groups in the **cellulose** ether to 37.6% by weight or
lower is effective for preventing the gelling aid (potassium chloride
in
these examples) from. . .
DETD There has been described a **cellulose** ether film in which the
cellulose ether used as the base has an optimum content of alkoxyl and
hydroxyalkoxyl groups, which is effective for preventing the gelling
aid
from precipitating out and maintaining a favorable outer appearance
during long-term storage. The **cellulose** ether film is thus suitable as
the shell of hard capsules for use in the pharmaceutical and health
food
fields.
CLM What is claimed is:
1. A hard capsule formed of a film composition comprising a
hydroxypropyl methyl **cellulose** as a base, a gelling agent, and a
gelling aid, wherein said hydroxypropyl methyl **cellulose** has a content
of hydroxypropyl groups of at least 4% by weight of the hydroxypropyl
methyl **cellulose** and a content of methoxyl groups and hydroxypropoxyl
groups combined of 23 to 37.4% by weight of the hydroxypropyl methyl
cellulose.

CLM What is claimed is:
. . . capsule formed of a film of claim 1, wherein said composition
contains 100 parts by weight of the hydroxypropyl methyl **cellulose**,
0.25 to 25 parts by weight of the gelling agent, and 0.25 to 25 parts
by
weight of the gelling. . .
CLM What is claimed is:
. . . claim 1, wherein the gelling agent is selected from the group
consisting of carrageenan, tamarind seed polysaccharide, pectin,
curdlan, furcellaran, **gellan gum**, and mixtures thereof.

CLM What is claimed is:
. . . 1, wherein the content of methoxyl and hydroxypropoxyl groups
combined is 28 to 37% by weight of the hydroxypropyl methyl **cellulose**.

L57 ANSWER 16 OF 79 USPATFULL on STN (Continued)

polyvinyl alcohol matrix may be activated by the introduction of
isocyanate functionalities via an 8 atom spacer. These activated beads
(N-PVA. . . .
SUMM . . . by PCR. Thus, after the microorganisms have bound to said
solid
support there will be a cell lysis step to **release** the nucleic acid
from the microorganisms for subsequent analysis. The **released** nucleic
acid may be analyzed in solution but is more conveniently analysed
after
it has bound to a solid support. . . .
SUMM [0061] (d) binding nucleic acid **released** from said lysed
microorganisms to a solid support.
SUMM [0063] Suitable methods for lysing the microorganisms, binding the
nucleic acid thus **released** and analysing the nucleic acid are provided
in WO98/31697 which is incorporated herein by reference. Thus, a
further
aspect of. . .
SUMM [0066] (d) binding nucleic acid **released** from said lysed cells to a
solid support;
SUMM [0070] (d) binding nucleic acid **released** from said lysed cells to a
solid support; and
SUMM [0073] Following binding, the isolated or support-bound microorganism,
are lysed to **release** their nucleic acid. The method of cell lysis are
well known in the art and widely described in the literature and. . .
SUMM [0074] Following lysis, the **released** nucleic acid is conveniently
bound to a solid support, preferably the one to which the lysed
microorganisms are bound. Although. . .
SUMM . . . solid support. Conveniently, the nucleic acid is bound
non-specifically to the support ie. independently of sequence. Thus,
for
example the **released** nucleic acid may be precipitated onto the support
using any of the known precipitants for nucleic acid, eg. alcohols,
alcohol/salt. . . beads in this manner is described for example in
WO
98/12079. Thus, salt may be added to the support and **released** nucleic
acid in solution, followed by addition of alcohol which will cause the
nucleic acid to precipitate. Alternatively, the salt. . .
SUMM . . . ge 968 ethanol, may simply be added to the mixture, and
incubated for a time period sufficient to allow the **released** nucleic
acid to become bound to the support. The incubation conditions for this
step are not critical and may simply. . .
SUMM . . . Depending on the support and the nature of any subsequent
processing desired, it may or may not be desirable to **release** the
nucleic acid from the support.
SUMM [0096] In amplification techniques such as PCR, the heating required in
the first step to melt the DNA duplex may **release** the bound DNA from
the support. This, in the case of a subsequent detection step, such as
PCR, the support. . . .
SUMM [0104] (d) means for binding nucleic acid **released** from said lysed
cells to a solid support;
DETD . . . an overnight culture using the beads of Examples 3,4 and 5 and
Dynabeads M-280 (Dynal, Norway) (unactivated). After lysis to **release**
nucleic acid, an E. coli DNA sequence of approximately 600 bp was
amplified using the primers 0597/1673 (see Table 1).
DETD [0212] After lysis to **release** nucleic acid, a B. cereus sequence of
approximately 600 bp was amplified using the primers 0557/1254 (see
Table 1). The. . .
DETD . . . be preferred as the sulphate group may inhibit the PCR

L57 ANSWER 16 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2003:219755 USPATFULL
TITLE: Cell isolation method
INVENTOR(S): Refsahl, Uge Hilde, Oslo, NORWAY
Holpus, Tove, Oslo, NORWAY

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 20030153028	A1	20030814	
APPLICATION INFO.:	US 2002-163998	A1	20021105 (10)	
	WO 2001-GB540		20010202	<--

	NUMBER	DATE	
PRIORITY INFORMATION:	GB 2000-1459	20000121	<--
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Janet M MacLeod, Dorsey & Whitney, 250 Park Avenue, New York, NY, 10177		
NUMBER OF CLAIMS:	26		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	11 Drawing Page(s)		
LINE COUNT:	1927		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a method of isolating cells from a sample which method comprises binding said cells to a solid support by means of a non-specific ligand immobilized on said solid support, particularly to a method of isolating microorganisms from a sample. Preferred ligands for use in such methods include carbohydrates and derivatives thereof. Also described is a kit for isolating microorganisms from a sample comprising: (a) a solid support having immobilized thereon a ligand which is capable of non-specific binding to
microorganisms; (b) means for binding microorganisms to said solid support; optionally (c) means for lysing said cells; and optionally (d) means for binding nucleic acid **released** from said lysed cells to a solid support.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AI 20010122

AB . . . microorganisms to said solid support; optionally (c) means for lysing said cells; and optionally (d) means for binding nucleic acid **released** from said lysed cells to a solid support.
SUMM . . . use in the method of the invention are available from Dyno Particles AS (Lillestr.0.m, Norway) as well as from Qiagen, **Pharmacia** and Serotec.
SUMM . . . use as a solid support in the methods of the invention are spherical shaped polymer particles **based** on PVA (**polyvinyl** alcohol) in which a magnetic colloid has been encapsulated. These beads may be produced through suspension of a polymer phase. . . .
SUMM . . . covalent attachment to the solid support. In the case of the superparamagnetic beads from Chemagen which are discussed above, the

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when
a **carrageenan coating** is used, the PCR is performed on the
supernatant following incubation of the beads at 80° C. to
release all the DNA from the beads.
DETD [0248] Well no 10-100 µl 10.sup.-2 dilution of V. cholerae added to
200 µg Chemagen **coated** with **Carrageenan**
DETD [0249] Well no 11-100 µl 10.sup.-2 dilution of V. cholerae added to
200 µg Chemagen **coated** with **Carrageenan**
DETD [0250] Well no 12-100 µl 10.sup.-4 dilution of V. cholerae added to
200 µg Chemagen **coated** with **Carrageenan**
DETD [0251] Well no 13-100 µl 10.sup.-5 dilution of V. cholerae added to
200 µg Chemagen **coated** with **Carrageenan**
DETD [0276] Well no 10-100 µl 10.sup.-2 dilution of S.flexneria added to
200 µg Chemagen **coated** with **Carrageenan**
DETD [0277] Well no 11-100 µl 10.sup.-2 dilution of S.flexneria added to
200 µg Chemagen **coated** with **Carrageenan**
DETD [0278] Well no 12-100 µl 10.sup.-4 dilution of S.flexneria added to
200 µg Chemagen **coated** with **Carrageenan**
DETD [0279] Well no 13-100 µl 10.sup.-5 dilution of S.flexneria added to
200 µg Chemagen **coated** with **Carrageenan**
DETD [0296] Well no 2-100 µl 10.sup.-1 dilution of E. coli added to 200
µg Chemagen beads **coated** with **Carrageenan**
DETD [0297] Well no 3-100 µl 10.sup.-2 dilution of E. coli added to 200
µg Chemagen beads **coated** with **Carrageenan**
DETD [0298] Well no 4-100 µl 10.sup.-3 dilution of E. coli added to 200
µg Chemagen beads **coated** with **Carrageenan**
DETD [0299] Well no 5-100 µl 10.sup.-4 dilution of E. coli added to 200
µg Chemagen beads **coated** with **Carrageenan**
DETD [0300] Well no 6-100 µl 10.sup.-5 dilution of E. coli added to 200
µg Chemagen beads **coated** with **Carrageenan**
DETD [0301] Well no 7-100 µl 10.sup.-6 dilution of E. coli added to 200
µg Chemagen beads **coated** with **Carrageenan**
DETD [0302] Well no 8-100 µl 10.sup.-7 dilution of E. coli added to 200
µg Chemagen beads **coated** with **Carrageenan**
DETD [0354] Well no 2-100 µl 10.sup.-1 dilution of S.typhimurium added to
100 µg Chemagen beads **coated** with **Carrageenan**
DETD [0355] Well no 3-100 µl 10.sup.-2 dilution of S.typhimurium added to
100 µg Chemagen beads **coated** with **Carrageenan**
DETD [0356] Well no 4-100 µl 10.sup.-3 dilution of S.typhimurium added to
200 µg Chemagen beads **coated** with **Carrageenan**
DETD [0357] Well no 5-100 µl 10.sup.-4 dilution of S.typhimurium added to
200 µg Chemagen beads **coated** with **Carrageenan**
DETD [0358] Well no 6-100 µl 10.sup.-5 dilution of S.typhimurium added to
200 µg Chemagen beads **coated** with **Carrageenan**
DETD [0359] Well no 7-100 µl 10.sup.-6 dilution of S.typhimurium added to
200 µg Chemagen beads **coated** with **Carrageenan**
DETD [0360] Well no 8-100 µl 10.sup.-7 dilution of S.typhimurium added to
200 µg Chemagen beads **coated** with **Carrageenan**
DETD [0441] Well no 32-100 µl 10.sup.-2 dilution of C. jejuni added to 200
µg Chemagen beads **coated** with **Carrageenan**
DETD [0442] Well no 33-100 µl 10.sup.-2 dilution of C. jejuni added to 200
µg Chemagen beads **coated** with **Carrageenan**
DETD [0443] Well no 34-100 µl 10.sup.-3 dilution of C. jejuni added to 200
µgChemagen beads **coated** with **Carrageenan**
DETD [0444] Well no 35-100 µl 10.sup.-4 dilution of C. jejuni added to 200
µg Chemagen beads **coated** with **Carrageenan**
DETD [0445] Well no 36-100 µl 10.sup.-5 dilution of C. jejuni added to 200

L57 ANSWER 16 OF 79 USPATFULL on STN (Continued)
ag Chemagen beads coated with Carrageenan
DETD [0446] Well no 37-705 µl 10.axp.-6 dilution of C. jejuni added to 200 µg Chemagen beads coated with Carrageenan
DETD [0488] Well no 3-199 µl 10.axp.-5 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0459] Well no 3e-199 µl 12.axp.-2 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0460] Well no 4e-200 µl 12.axp.-3 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0491] Well no 5e-200 µl 12.axp.-4 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0492] Well no 6e-200 µl 12.axp.-5 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0493] Well no 7e-200 µl 10.axp.-4 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0494] Well no 8e-125 µl 12.axp.-4 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0495] Well no 9e-125 µl 12.axp.-6 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0496] Well no 10e-900 µl 10.axp.-3 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0499] Well no 11e-200 µl 10.axp.-2 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0500] Well no 37e-200 µl 10.axp.-4 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0501] Well no 14e-200 µl 10.axp.-5 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0502] Well no 15-200 µl 10.axp.-6 dilution of S.pyogenes added to 200 µg Chemagen beads coated with Carrageenan
DETD [0514] Well no 1e-200 µl 12.axp.-1 dilution of N.gonorrhoeae added to 200 µg Chemagen beads coated with Carrageenan
DETD [0515] Well no 2e-200 µl 12.axp.-2 dilution of N.gonorrhoeae added to 200 µg Chemagen beads coated with Carrageenan
DETD [0516] Well no 3e-200 µl 12.axp.-3 dilution of N.gonorrhoeae added to 200 µg Chemagen beads coated with Carrageenan
DETD [0553] Well no 1e-200 µl 10.axp.-4 dilution of N.gonorrhoeae added to 200 µg Chemagen beads coated with Carrageenan
DETD [0554] Well no 2e-200 µl 10.axp.-5 dilution of N.gonorrhoeae added to 200 µg Chemagen beads coated with Carrageenan
DETD [0555] Well no 4e-200 µl 10.axp.-6 dilution of N.gonorrhoeae added to 200 µg Chemagen beads coated with Carrageenan
DETD [0556] Well no 5e-200 µl 12.axp.-4 dilution of N.gonorrhoeae added to 200 µg Chemagen beads coated with Carrageenan
DETD [0557] Well no 6e-200 µl 12.axp.-5 dilution of N.gonorrhoeae added to 200 µg Chemagen beads coated with Carrageenan
DETD [0558] Well no 9e-200 µl 10.axp.-6 dilution of N.gonorrhoeae added to 200 µg Chemagen beads coated with Carrageenan
DETD [0575] Well no. 2e-200 µl 10.axp.-2 dilution of B-cells added to 200 µg chemagen beads coated with Type V carrageenan
DETD [0576] Well no. 3e-200 µl 10.axp.-3 dilution of B-cells added to 200 µg chemagen beads coated with Type V carrageenan
DETD [0577] Well no. 4e-200 µl 10.axp.-4 dilution of B-cells added to 200 µg chemagen beads coated with Type V carrageenan
DETD [0578] Well no. 5e-200 µl 10.axp.-5 dilution of B-cells added to 200

L57 ANSWER 16 OF 79 USPATFULL on STN (Continued)
µg chemagen beads coated with Type V carrageenan
DETD [0581] Well no. 2e-200 µl 10.axp.-0 dilution of B-cells added to 200 µg Dynabeads coated with Type I carrageenan
DETD [0582] Well no. 3e-200 µl 10.axp.-1 dilution of B-cells added to 200 µg Dynabeads coated with Type I carrageenan
DETD [0583] Well no. 4e-200 µl 10.axp.-2 dilution of B-cells added to 200 µg Dynabeads coated with Type I carrageenan
DETD [0584] Well no. 5e-200 µl 10.axp.-3 dilution of B-cells added to 200 µg Dynabeads coated with Type I carrageenan
DETD [0587] Well no. 2e-200 µl 10.axp.-0 dilution of B-cells added to 200 µg Dynabeads coated with Type II carrageenan
DETD [0588] Well no. 3e-200 µl 10.axp.-1 dilution of B-cells added to 200 µg Dynabeads coated with Type II carrageenan
DETD [0589] Well no. 4e-200 µl 10.axp.-2 dilution of B-cells added to 200 µg Dynabeads coated with Type II carrageenan
DETD [0590] Well no. 5e-200 µl 10.axp.-3 dilution of B-cells added to 200 µg Dynabeads coated with Type II carrageenan
DETD [0593] Well no. 2e-200 µl 10.axp.- dilution of B-cells added to 200 µg Dynabeads coated with Type V carrageenan.
DETD [0594] Well no. 3e-200 µl 10.axp.-1 dilution of B-cells added to 200 µg Dynabeads coated with Type V carrageenan
DETD [0595] Well no. 4e-200 µl 10.axp.-2 dilution of B-cells added to 200 µg Dynabeads coated with Type V carrageenan
DETD [0596] Well no. 5e-200 µl 10.axp.-3 dilution of B-cells added to 200 µg Dynabeads coated with Type V carrageenan
CLM What is claimed is:
13. A method as claimed in claim 11 or claim 12 wherein the bound cells are lysed to **release** their nucleic acid.
CLM What is claimed is:
14. A method as claimed in claim 13 wherein the **released** nucleic acid is bound to a solid support.
CLM What is claimed is:
17. A method as claimed in claim 16 wherein the nucleic acid **released** from said lysed microorganisms is bound to a solid support.
CLM What is claimed is:
. . . means of a non-specific ligand immobilised on said solid support; (b) lysing the bound cells; and (c) binding nucleic acid **released** from said lysed cells to a solid support.
CLM What is claimed is:
. . . by means of a non-specific ligand immobilised on said solid support; (b) lysing the bound cells; (c) binding nucleic acid **released** from said lysed cells to a solid support; and (d) detecting the presence or absence of nucleic acid characteristic of. . .
CLM What is claimed is:
. . . microorganisms to said solid support; optionally (c) means for lysing said cells; and optionally (d) means for binding nucleic acid **released** from said lysed cells to a solid support.

L57 ANSWER 17 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2003:123027 USPATFULL
TITLE: Granule with hydrated barrier material
INVENTOR(S): Secker, Nathaniel T., Bellingham, CA, United States
Christensen, Jr., Robert I., Pinole, CA, United States
Gaertner, Alfred L., San Bruno, CA, United States
Ghani, Mahmood M., Milpitas, CA, United States
Dale, Douglas A., Pacifica, CA, United States
PATENT ASSIGNEE(S): Genencor International, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6602841	B1	20030805	
	WO 9932295		19990701	<--
APPLICATION INFO.:	US 2000-581717		20000614 (9)	<--
	WO 1998-US27214		19981221	<--

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1997-68382P	19971220 (60)	<--
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Dawson, Lorna M.		
LEGAL REPRESENTATIVE:	Genencor International, Inc.		
NUMBER OF CLAIMS:	22		
EXEMPLARY CLAIM:	1,9		
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)		
LINE COUNT:	492		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A granule having high stability and low dust is described. The granule includes a hydrated barrier material having moderate or high water activity. Also described are methods of producing the granules.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AI 19981221

SUM01 U.S. Pat. No. 4,106,991 describes an improved formation of enzyme granules by prilloding within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-40% w/w based on the dry weight of the whole composition. In addition, this patent. . .
SUM01 . . . diatomaceous earth or sodium nitrate crystals. The film forming material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.
SUM01 . . . and improved stability formulations. Accomplishing all these desired characteristics simultaneously is a particularly challenging task since, for example, many delayed **release** or low-dust agents such as fibrous **cellulose** or waxy micro polymers leave behind insoluble residues.
SUM01 Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as enzymes.
SUM01 Suitable coatings include **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose**, hydroxypropylmethyl **cellulose**, **hydroxycellulose**, **ethylcellulose**,

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carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan, **carrageenan**, latex polymers, and esterize **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.
SUM01 . . . Preferably, the outer coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVA-methylmethacrylate copolymer and PVP-PVA copolymer.
DETD Finally, a polymer coating solution was prepared by dissolving 6.35 kg of Elvanol 51-05 **polyvinyl** alcohol, 7.94 kg titanium dioxide and 1.59 kg Neodol 23-6.5T nonionic surfactant in 50.12 kg water and spraying over the. . .

L57 ANSWER 18 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2003:187493 USPATFULL
TITLE: Edible MCC/PGA coating composition
INVENTOR(S): Acquella, Michael, Malaga, NJ, UNITED STATES
Dell, Sheila M., New Hope, PA, UNITED STATES
Silleferich, Eric H., Yardville, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003122339	A1	20030703
APPLICATION INFO.:	US 2002-304449	A1	20021127 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2000-496780, filed on 26 Oct 2000, ABANDONED, Pat. No. US 6500462		

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-162514P	19991029 (60)	<--
	US 1999-162707P	19991126 (60)	<--
	US 1999-172598P	19991221 (60)	<--
	US 2000-185588P	20000315 (60)	<--
	US 2000-213479P	20000711 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WOODCOCK WASHBURN LLP, ONE LIBERTY PLACE, 46TH FLOOR, 1650 MARKET STREET, PHILADELPHIA, PA, 19103

NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
LINE COUNT: 675
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable coating composition is disclosed containing microcrystalline **cellulose**, a film forming amount of propylene glycol alginate, and a strengthening polymer, optionally in combination with at least one of a plasticizer, a surfactant, or a filler. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable coating composition is disclosed containing microcrystalline **Cellulose**, a film forming amount of propylene glycol alginate, and a strengthening polymer, optionally in combination with at least one of a plasticizer, a surfactant, or a filler. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

SUMM [0002] This invention relates to edible, hardenable coating compositions

L57 ANSWER 18 OF 79 USPATFULL on STN (Continued)
immediate dissolution of active ingredients from tablets or other solid dosage forms coated with them. Thus, they provide prompt **release** or dissolution consistent with the release rates which are normally obtained with the uncoated tablets or other substrate. They do not, when

placed in water or ingested, adversely impact or retard **release** or dissolution of tablets or other solid dosage forms coated with them. Coatings made in accordance with the present invention are.

SUMM [0015] The microcrystalline **cellulose**, preferably admixed with propylene glycol alginate, provides important film characteristics required to provide an elegant coating which is particularly useful in, for example,

coating **pharmaceutical** and veterinary tablets, caplets, granules, and spheres which contain active ingredients which require **release** promptly after being placed in an aqueous media or ingested.

SUMM [0016] Microcrystalline **cellulose** is a purified, partially depolymerized **cellulose** that usually prepared by treating a source of **cellulose**, preferably alpha **cellulose** in the form of a pulp from fibrous plants, with a mineral acid, preferably hydrochloric acid. The acid selectively attacks the less ordered regions of the **cellulose** polymer chain, thereby exposing and freeing the crystallite sites, forming the crystallite aggregates which constitute microcrystalline **Cellulose**. These are then separated from the reaction mixture and washed to remove degraded by-products. The resulting wet mass, generally containing.

SUMM [0019] Propylene glycol alginate may be used in combination with other film forming materials, for example, carrageenan and **cellulosic** polymers such as HPMC and **hydroxypropylcellulose**.

SUMM . . . glycol alginate at a concentration in the range of about 3% to about 20% of the dry weight of the **coating** composition. When **carrageenan** is employed in the composition at a concentration in the range of about 3% to about 8%, it is believed.

SUMM [0022] The weight ratio of microcrystalline **cellulose** to propylene glycol alginate in the compositions of this invention may vary depending

on the application, but generally range from.

SUMM [0024] A dry, physical blend of microcrystalline **cellulose** and a film forming amount of propylene glycol alginate, a strengthening polymer, preferably, **hydroxyethylcellulose** (HEC), are present in the coating formulation of this invention and may be used in combination with other optional ingredients such as a. . . combinations thereof. Other strengthening polymers which can provide the same benefit and may be used instead of HEC include HPMC, **hydroxypropylcellulose**, **ethylcellulose**, **methylcellulose** and **polyvinylpyrrolidone** (PVP), however care must be exercised in the use of such alternative materials to avoid retarding **release** of active ingredients and/or bioavailability.

SUMM [0024] The preferred amount of strengthening polymer is less than the total amount of microcrystalline **cellulose** and propylene glycol alginate present in the composition. Depending on the desired hardness of the coating, the strengthening polymer may . . . another strengthening polymer is included in the formulation. Strengthening polymers suitable for use in this invention, which will not retard **release** from tablets or other solid dosage forms, are those polymers having a viscosity equal to or less than 20 mPa.multidot.s. . . . On a dry weight percentage basis the composition of this invention comprises from about 15% to about 50% of microcrystalline **cellulose**, about 10% to about 50% by weight of propylene glycol

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comprising microcrystalline **cellulose** (MCC), a film forming amount of propylene glycol alginate (PGA) and a strengthening polymer, optionally containing a plasticizer, a surfactant, a coloring agent or a combination of such optional ingredients. The coatings of the present invention can be applied to **pharmaceutical**, including neutraceutical, and veterinary solid dosage forms, such solid substrates such as seeds, animal feed, fertilizers, pesticide tablets and granules, dispersed in aqueous media, and, when applied as a coating, provide high

lustre coatings, which do not retard or extend **release** of active ingredient from a coated substrate.

SUMM [0003] It is a common practice to coat **pharmaceutical** and veterinary tablets to obtain several advantages. Among these are to improve the surface characteristics of tablets to make them.

SUMM [0004] Another very important function of a **pharmaceutical** or veterinary tablet coating is to improve the integrity of the tablet itself. Uncoated tablets are often subject to being. . .

SUMM [0011] A particular disadvantage of tablets coated heretofore usually on **hydroxypropylmethylcellulose** (HPMC) is that the coating may harden over time and therefore increase total disintegration time. An increase in disintegration time. . . proportion to the increase in disintegration time. Many other agents commonly used in coating compositions are also known to delay **release** of **pharmaceutical** agents, such as stearic coating materials which use hydrophobic forming materials which are insoluble in water, or gastric fluid, some of these being specifically selected to by-pass both the stomach and small intestine and provide colonic **release**.

SUMM [0012] The coatings of this invention meet U.S. **Pharmacopeia** standards for rapid or immediate dissolution (U.S.P. monograph 23) of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates. Thus, they do not adversely impact or retard **release** of active ingredients from a substrate coated with them. Further, the coatings of this invention are readily dispersed and rapidly. . . . . in accordance with the present invention by a coating composition which comprises a unique combination of materials specifically adapted for prompt **release** when placed in aqueous media or ingested. The coating composition of the present invention comprises microcrystalline **cellulose**, a film forming amount of propylene glycol alginate, a strengthening polymer, and may additionally contain a plasticizer, a surface. . . agent, a filler, a coloring agent or combination of these additional ingredients. More specifically, the present invention provides a prompt **release**, edible, hardenable coating composition, as well as dry coatings and aqueous dispersions thereof and solid dosage forms coated therewith.

SUMM . . . application, the term "edible" is intended to mean food grade materials which are approved by regulatory authorities for use in **pharmaceutical** or food applications. The term "hardenable," used to describe the coating compositions of this invention, is intended to include only. . . . this invention or tablets coated with the compositions of this invention, mean that the coatings of this invention

meet U.S. **Pharmacopeia** standards (U.S.P. monograph 23) for rapid or

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alginate, and about 5% to about 25% of strengthening polymer. . . . may be preferable to maintain agitation of the aqueous dispersion during the period of its use in being sprayed on the **pharmaceutical** or veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizer, pesticide tablets, or.

SUMM [0031] The preferred edible, hardenable, prompt **release** coating formulations of the invention may generally be prepared and used according to a simple procedure. A dry blend of microcrystalline **cellulose** and propylene glycol alginate, a strengthening polymer, such as **hydroxypropylcellulose**, and optionally at least one additional ingredient, such as **pharmaceutical** or other acceptable plasticizer,

optionally together with a solid. . . .

SUMM [0032] In the formulations of microcrystalline **cellulose** and propylene glycol alginate, a simple propylene glycol alginate solvent system for rapid hydration. The period of hydration may be. . . thixotropic behavior of a formulation which sets up during overnight storage.

Unlike

coating formulations based primarily on hydroxyalkyl ethers of **cellulose**, for example, HPMC, constant stirring of the microcrystalline and propylene glycol alginate formulations of this invention does not need to.

SUMM . . . variables which can be utilized in the art can manipulate to provide an elegant coating based on dry blends of microcrystalline **cellulose** and propylene glycol alginate, include inlet temperature, outlet temperature, air flow, speed of rotation of the coating pan, and the.

SUMM [0034] **Hydroxypropylcellulose** binds water more effectively than propylene glycol alginate does. Thus, the presence of the water amount propylene glycol alginate in. . . glycol alginate which dilutes the negative effect of HEC on drying time. Although, in the case of coating active **pharmaceutical** agents, for example, ibuprofen, the outlet temperature can be reduced and still provide short enough drying time to

be commercially.

SUMM [0035] **Hydroxyethylcellulose** is particularly susceptible to clogging spray nozzles at high temperatures. An additional benefit provided by the formulations of this invention is that

SUMM [0036] The level of coating applied to **pharmaceutical** or veterinary dosage forms is preferably between about 2% to 15% by weight of the uncoated dosage form, more.

. . . . a substrate for coating. This is an additional unexpected benefit of the coatings based on propylene glycol alginate and microcrystalline **cellulose**, and it differs from the known drawbacks of coating formulations in which HPMC is the primary or only film-former.

SUMM [0041] All components of the formulation are typically **pharmaceutically** acceptable, edible food grade materials.

DETD [0043] In a Patterson-Kelly twin shell blender were placed 48.0 grams of

a blend of microcrystalline **cellulose** (Avicel® PH-105, 35 grams) and propylene glycol alginate (13 grams), 20 grams of **hydroxypropylcellulose** (Aqualon®-L, 25 grams of triacetin, and 3 grams of Fluronic F-68 (BASF). After the dry components had been thoroughly blended,.

DETD . . . 1 below:

TABLE 1

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Example:	3	4	5
	2		
Ingredients	Weight (grams)		
Avicel PH-105	37	37	37
Hydroxyethyl-cellulose	22	22	22
FDA.sup.a	13	13	12
Fluronic F-68	3.5	3	1.5
Red #40	24 5	6	7.5
dispersion			
Triacetin	--	25	--
Mannitol.sup.b	--	--	18
Iota	--	--	5
carrageenan			
Deionized water	1011.1	1011.1	1011.1
Hydration time	2 hours	>1 hour	6 hours
Caplets	Charge (Kg)		
Acetaminophen	0.67	1	0.67
Ibuprofen	0.67		0.67

DETD . . . friability. This example is summarized in Table 2:

TABLE 2

Example:	6
Ingredients	Weight (grams)
Avicel PH-105	37
FDA.	**13**
Iota **carrageenan**	5
Hydroxyethylcellulose	**22**
Mannitol.sup.b	17.5
Fluronic F-68	3.5
Blue Lake #2	2
Deionized water	1350
Hydration time	2 hours
Caplets	Charge (Kg
Ibuprofen. . .	

DETD . . . 35

KEC		20	10	5	--
--					
15	15				
Lecithin.sup.b		3	3	3	-- 3
3	3				
Maltodextrin M180		17	17	17	25
22	**17**	**17**			
Iota **Carrageenan**		5	5	5	5
5	5	5			
Red No&eqhalIe Iron Oxide		5	5	5	--
15					
30	--				

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ACCESSION NUMBER: 2003:158994 USPATFULL
TITLE: Film forming compositions containing sucralose
INVENTOR(S): Szymczak, Christopher E., Marlton, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20030108607	A1	20030612
APPLICATION INFO.:	US 2002-176832	A1	20020621 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-325727P	20010928 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	ANTHONY A. CIAMPOCERO JR., JOHNSON & JOHNSON, ONE JOHNSON & JOHNSON PLAZA, NEW BRUNSWICK, NJ, 08933-7003	
NUMBER OF CLAIMS:	33	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Page(s)	
LINE COUNT:	995	

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Water soluble, gelatin-free dip coatings for substrates comprising a hydrocolloid, such as carrageenan, and sucralose.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM . . . to capsule products are caplets, which generally are solid, oblong tablets that are often coated with various polymers such as **cellulose** ethers to improve their aesthetics, stability, and swallowability. Typically, such polymers are applied to the tablets either from solution in . . .

SUM . . . shells via conventional dip molding processing. See also U.S. Pat. No. 6,001,202 (capsules prepared via pin dip coating with thermogelled **methylcellulose** ether compositions). However, due to potential tampering concerns, hard gelatin capsules are no longer a preferred delivery system for . . .

SUM . . . to 5 percent by weight of the hydrocolloids as a "setting system" in combination with known film-forming polymers such as **polyvinyl** alcohol, starch ethers, or oxidized starch.

SUM . . . [0012] One hydrocolloid, **carrageenan**, has been used in film **coatings** for pharmaceutical applications. However, **carrageenan** by itself was considered to be too weak for coating pharmaceutical tablets, and thus was required to be combined with microcrystalline **cellulose** for satisfactory coating results. See WO 00/45794. Not only is the addition of the **cellulose** to the carrageenan not economically advantageous, but the viscosity of the resulting mixture is also difficult to control. Moreover, the inclusion of the **cellulose** as such coatings tends to hinder the overall dissolution rate of the coating, which thereby delays

the release time of. . .

DETD . . . and 6,274,162, which are all incorporated by reference herein. Additional suitable subcoatings include one or more of the following ingredients: **cellulose** ethers such as **hydroxypropylmethylcellulose**, **hydroxypropylcellulose**, and **hydroxyethylcellulose**; polycarbohydrates such as xanthan gum, starch, and maltodextrin; plasticizers including for example, glycerin, polyethylene glycol, propylene glycol, dibutyl

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Blue Lake/Yellow Lake blend. . .

DETD . . . 22 25 25 25

FDA.sup.a	35	35	30	13	26	25	25	13	13	13	20
	18	26	20	15	20						
Hydroxyethylcellulose	15	15	17	20	22	22	20	20	20	20	17
	15	20	**15**	**20**	**20**						
Iota **carrageenan**	5	5	5	5	5	12	12	12	15	15	12
	12	12	12	10	10						
Lecithin.sup.b	3	3	3	5	. .						

CLM What is claimed is:

1. An edible, hardenable, prompt-release coating composition comprising (a) microcrystalline **cellulose**, (b) a film forming amount of propylene glycol alginate, (c) a strengthening polymer and optionally

(d) at least one of. . .

CLM What is claimed is:

2. The coating composition of claim 1, comprising 5% to 50% by weight microcrystalline **cellulose**, 10% to 50% by weight propylene glycol alginate, and 5% to 25% by weight strengthening polymer.

CLM What is claimed is:

4. The coating composition of claim 1 in which the strengthening polymer

is **hydroxyethylcellulose**.

CLM What is claimed is:

10. The coating composition of claim 1, in which the weight ratio of microcrystalline **cellulose** to propylene glycol alginate is in the range of 90:10 to 20:80.

CLM What is claimed is:

11. The coating composition of claim 1, wherein the microcrystalline **cellulose** has an average particle size in the range of 1 to 50 microns.

CLM What is claimed is:

12. The coating composition of claim **10**, further comprising **carrageenan** in an amount of from 3% to 20% by dry weight of the composition.

CLM What is claimed is:

13. The **coating** composition of claim **12**, wherein **carrageenan** is present in an amount in the range of 3% to 8% by dry weight of the composition and the. . .

CLM What is claimed is:

14. The composition of claim **12** wherein **carrageenan** is present in an amount in the range of 9% to 20% by dry weight of the composition and the. . .

CLM What is claimed is:

19. A method for forming an edible, hardenable, prompt **release** coating composition comprising (a) combining (a) microcrystalline **cellulose**, (b) a film forming amount of propylene glycol alginate, (c) a strengthening polymer and optionally (d) at least one of. . .

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edecate, triethyl. . .

DETD . . . from about 2 percent to about 8 percent, e.g. from about 4 percent to about 6 percent of a water-soluble **cellulose** ether and from about 0.1 percent to about 1 percent castor oil, as disclosed in detail in U.S. Pat. No. . .

DETD . . . methenamine mandelate; menthol; meperidine hydrochloride; metaproterenol sulfate; methocopolamine and its nitrates; methenzide and its maleate; methyl nicotinate; methyl salicylate; methyl **cellulose**; methsuximide; metoclopramide and its halides/hydrates; metronidazole; metoprotol tartrate; miconazole nitrate; mineral oil; minoxidil; morphine; naproxen and its alkali metal salts; . . .

DETD . . . component, forms an effective film coating on substrates in the

substantial absence of a film former or strengthening polymer, e.g., **cellulose**, starches, pullulan, **polyvinylpyrrolidone**, derivatives thereof, and mixtures thereof. Examples of such **cellulosics** include, but are not limited to, **hydroxypropylmethylcellulose**, microcrystalline **cellulose**, **hydroxyethylcellulose**, **hydroxypropylcellulose**, **ethylcellulose**, **cellulose** acetate, and mixtures thereof. By "substantial absence" it is meant less than, based upon the total weight

of the film. . .

DETD [0079] 4. Dip **Coating** Substrates with a Sucralose-**Carrageenan** Dispersion

DETD [0073] 5. Dip **Coating** Substrates with a Sucralose-**Carrageenan** Dispersion

DETD [0076] 6. Preparation of Sucralose-Kappa **Carrageenan** Dispersion, and Tablets **coated** therewith.

DETD [0082] 7. Preparation of Sucralose-Iota/Kappa **Carrageenan** (mixture) Dispersion, and Tablets **coated** therewith.

CLM What is claimed is:

15. The coated dosage form of claim 14 wherein the subcoating comprises **cellulose** ethers, plasticizers, polycarbohydrates, pigments, opacifiers, and mixtures thereof.

CLM What is claimed is:

30. The medicament of claim 29 wherein the subcoating comprises materials selected from the group consisting of **cellulose** ethers, plasticizers, polycarbohydrates, pigments, opacifiers, and mixtures thereof.

CLM What is claimed is:

32. The film forming composition of claim 31 wherein the film former is selected from the group consisting of **cellulose**, starch, **polyvinylpyrrolidone**, derivatives and mixtures thereof.

L57 ANSWER 20 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2007:151820 USPATFULL
TITLE: Dog coating compositions containing starch or dextrin
INVENTOR(S): Gallay, Cynthia, Lansdale, PA, UNITED STATES
Gowan, Walter G., JR., Woodstock, GA, UNITED STATES
Szpurka, Christopher, Raritan, NJ, UNITED STATES
Papalia, Michelle, Philadelphia, PA, UNITED STATES
Chen, Jen-Chi, Morrisville, PA, UNITED STATES
Bunick, Frank J., Randolph, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2007207273	A1	20070607
APPLICATION INFO.:	US 2002-122531	A1	20020415 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-283127P	20010515 (60) <--
	US 2001-283128P	20010328 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Philip B. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003	
NUMBER OF CLAIMS:	35	
EXEMPLARY CLAIM:	1	
LINE COUNT:	1620	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Water soluble, gelatin-free dip coatings for tablets and capsules comprising sucrose, glycerin and pre-gelatinized waxy maize and/or tapioca dextrin or comprising hydroxypropyl starch, thickener, and plasticizer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . [0072] drugs. The ability to combine capsule halves having different colors provided manufacturers with a unique means of distinguishing various **pharmaceutical** products. Many patients preferred capsules over tablets, considering them as being easier to swallow. This consumer preference prompted **pharmaceutical** manufacturers to market capsules in various colors even when they were also available in tablet form.

SUMM . . . Alternative to capsule products are caplets, which are solid, oblong tablets that are often coated with various polymers such as **cellulose** ethers to improve their aesthetics, stability, and swallowability. Typically, such polymers are applied to the tablets either from solution in.

SUMM [0007] However, the use of gelatin as a **pharmaceutical** coating material presents certain disadvantages and limitations, including the potential for decreased dissolution rate after extended storage due to cross-linking.

SUMM . . . shells via conventional dip molding processing. See also U.S. Pat. No. 6,001,211 (capsules prepared via dip molding with thermogelled **methylcellulose** ether compositions). However, due to potential tampering concerns, hard gelatin capsules are no longer a

L57 ANSWER 20 OF 79 USPATFULL on STN (Continued)
xanthan gum, **gellan gum**, maltodextrin, galactomannan, pusztulan, laminarin, scleroglucan, gum arabic, inulin, pectin, whelan, chitosan, mannan, methylan, elsinan, cycloinulo-oligosaccharide, gelling starches such.

SUMM [0037] Any plasticizer known in the **pharmaceutical** art is suitable for use in the present invention, and may include, but not be limited to polyethylene glycol, glycerin, sorbitol, . . . gums and mixtures thereof. Suitable sugar-alcohols include xarbatol, mannitol, xylitol, malitol, erythritol, lactitol, and mixtures thereof. In addition, maintaining a **cellulose** ether film former, an optional plasticizer may be present in an amount, based upon the total weight of the solution,.

SUMM [0040] In embodiments wherein a **cellulose** ether film former is used in the composition, the film forming composition for dip coating substrates

may be substantially free.

SUMM . . . than about 100 percent, e.g. from about 95 percent to about 99.5 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.5 percent to about 5 percent, of a thickener, e.g., from about 97 percent to about 100

SUMM . . . is a chemically modified starch, the thickener may be selected from the group consisting of kappa or iota carrageenan, maltodextrin, **gellan gum**, agar, gelling starch and derivatives and mixtures thereof.

SUMM . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g.,

SUMM . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and is substantially free of hydrocolloids, i.e., e.g. contains less than about 1%, or less than about 0.01% of hydrocolloids.

SUMM . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.1 percent to about 1.0 percent, e.g. from about 0.25 percent to about 0.5 percent of a.

SUMM . . . to about 90 percent, e.g. from about 80 percent to about 90 percent of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 10 percent to about 80 percent, e.g. from about 5 percent to about 50 percent or from about.

SUMM . . . percent to about 15 percent or from about 10 percent to about 14 percent, of a film former such as **hydroxypropylmethylcellulose** and from about 85 percent to about 90 percent, e.g. from about 86 percent to about 0.16 percent or from.

SUMM . . . percent to about 25 percent or from about 20 to about 24 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**,

SUMM . . . percent to about 20 percent or from about 10 to about 18 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.001 percent to about 0.1 percent, e.g. from about 0.01 percent to about 0.09 percent of a.

L57 ANSWER 20 OF 79 USPATFULL on STN (Continued)
SUMM . . . to about 19 percent or from about 16 percent to about 19 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, from about 0.1 percent to about 17 percent, e.g. from about 1 percent to about 11 percent or from about.

SUMM . . . opacifying agents such as titanium dioxide, and/or from about 0

percent to about 14 percent colorants. See Remington's Practice of **Pharmacy**, Martin & Cook, 17.Aup.th ed., pp. 1625 - 30, which is herein

incorporated by reference.

SUMM [0060] Any coloring agent suitable for use in **pharmaceutical** applications may be used in the present invention and may include, but not be limited to azo dyes, quinophalone dyes,.

SUMM [0062] In one embodiment, the **pharmaceutical** dosage form is comprised of a) a core containing an active ingredient; b) an optional first coating layer comprised of.

SUMM and 6,274,162, which are all incorporated by reference herein. Additional suitable embodiments of the present invention are the following ingredients: **cellulose** ethers such as **hydroxypropylmethylcellulose, hydroxypropylcellulose**, and hydroxyethylcellulose; polysaccharides such as xanthan gum, starch, and maltodextrin; plasticizers including for example, glycerin, polyethylene glycol, propylene glycol, dibutyl sebecate, triethyl.

SUMM . . . from about 2 percent to about 8 percent, e.g. from about 4 percent to about 6 percent of a water-soluble **cellulose** ether and from about 0.1 percent to about 1 percent, castor oil, as disclosed in detail

in U.S. Pat. No. .

SUMM [0069] In one embodiment, the film former is a **cellulose** ether such as HPMC, and the thickener is a hydrocolloid such as xanthan gum and the weight gain enhancer is.

SUMM . . . any material that can be carried by or entrained in the system. .

For example, the active agent can be a **pharmaceutical**, nutraceutical, vitamin, dietary supplement, nutrient, flavor, foodstuff, edible, nutritional, mineral, supplement, or favoring agent or the like and combinations thereof.

SUMM . . . methenamine mandelate; menthol; naproxidan hydrochloride; netagocrotetel sulfate; methoglucamine and its nitrate; methotrexate and its maleate; methyl nisoxinate; methyl salicylate; methyl **cellulose**; methsuximide; metoclopramide and its hydrochloride; metrenbudazole; metoprotol tartrate; midecamole nitrate; mineral oil; minocullj morphine; naproxen and its potassium salt; magnesium . . . of active drug on a magnesium trisilicate base and on a magnesium aluminum

silicate base, and mixtures thereof. Mixtures and **pharmaceutically** acceptable salts of these and other actives can be used.

SUMM [0076] In one embodiment, the dosage forms coated with the dip coatings of the present invention provided for immediate **release** of the active ingredient, i.e. the dissolution of the dosage form conformed to USP specifications for immediate **release** tablets containing the particular active ingredient employed. For example, for acetaminophen tablets, USP 24 specifies that in pH 5.8 phosphate. . . . using USP apparatus 2 (paddles) at 50 rpm, at least 80% of the acetaminophen contained in the dosage form is **released** therefrom within 30 minutes after dosing, and

L57 ANSWER 20 OF 79 USPATFULL on STN (Continued)
for ibuprofen tablets, USP 24 specifies that in pH 7.2 phosphate buffer, . . .
using USP apparatus 2 (paddles) at 50 rpm, at least 80% of the ibuprofen . . .
contained in the dosage form is **released** therefrom within 60 minutes after dosing. See USP 24, 2000 Version, 19-20 and 856 (1999). . . .
SUMM . . . retained acceptable dissolution characteristics for the desired . . .
shelf-life and storage period at elevated temperature and humidity conditions. In particular, these **cellulose**-ether based compositions according to the present invention were also advantageously more resistant to microbial growth, which thereby enabled a longer. . . .
other dipping dispersions of the present invention may have been higher than that typically found in gelatin-based dipping solutions, the **cellulose**-ether based compositions of the present invention surprisingly required a shorter drying cycle time relative to that for gelatin-containing compositions. Third, . . .

DETD	. . . 212.3	564.67	564.67	564.67	564.67
maltodextrin	0	53	53	67	67
PEG 400	0	7	7	5	5
Hydroxy	0	0	0	0	0

ethylcellulose'

Total coating solution	233.3	666.67	666.67	666.67	666.67
Wt % solids in coating solution	9%	15%	15	15	15

'Available from Aqualon, under the tradename, "Natrosol. . . .

DETD	. . . ml)	0	0	0.13
	HPMC (1910, 5 mPas)	0	0	32.4
	PEG 400	5	5	0
	Hydroxy-	24	24	0

ethylcellulose'

Total coating solution	666.67	666.67	722.9	
Wt % solids in coating solution	15%	15%	4.5%	

'Available from Aqualon, under the tradename, . . .
DETD [0176] 88.4 kg (9% w/w) of hydroxypropyl **methylcellulose** 2910, 5 mPa s and 0.747 kg (0.24% w/w) of castor Oil were mixed into 593.8 kg (91 % w/w) of. . . .
DETD Preparation of Tablets Dip **Coated** with HPMC/**Carrageenan** Dipping Solutions
DETD . . . Motor fitted with a 4 cm propeller blade at a speed of 650 rpm for 30 minutes. 7.5 g of **Gellan Gum** ("Kelco gel", Kelco) was then added thereto with constant mixing for 15 min. 2.6 g of colorant ("Capsint Red ID-1762". . . . in Table 0:
TABLE 0

L57 ANSWER 20 OF 79 USPATFULL on STN (Continued)
Hydroxypropyl Starch Based Dipping Solutions

Component	Trade name	Supplier	Amount Used*
Hydroxypropyl Starch	Pure-Cote B790	Grain Processing Corporation	92.5
Gellan Gum	Kelcogel	Kelco	3.5
Colorant	Capsint Red	Colarcon	2.0
Water	N/A	N/A	300

*All values expressed in terms of weight (grams) unless otherwise stated

CLM What is claimed is:
. . . a) a hydroxypropyl starch film former; b) a thickener selected from the group consisting of kappa carrageenan, iota carrageenan, maltodextrin, **gellan gum**, agar, gelling starch, and derivatives and mixtures thereof; and c) a plasticizer, wherein the composition comprises a surface gloss of. . . .

CLM What is claimed is:
12. A **pharmaceutical** dosage form comprising an outer coating of the composition of claim 7.

CLM What is claimed is:
13. A **pharmaceutical** dosage form comprising a core, a subcoating substantially covering said core, and an outer coating substantially covering said subcoating, wherein. . . .

CLM What is claimed is:
14. The dosage form of claim 13 wherein the subcoating is selected from the group consisting of hydroxypropylmethyl **cellulose**, castor oil, maltodextrins, polyethylene glycol, polysorbate 80, and mixtures thereof.

CLM What is claimed is:
. . . comprised of, based upon the total dry weight of the subcoating, a) from about 2 percent to about 8 percent **hydroxypropylmethylcellulose,** and b) from about 0.1 percent to about 1 percent castor oil.

CLM What is claimed is:
. . . comprised of, based upon the total dry weight of the subcoating, a) from about 25 percent to about 40 percent **hydroxypropylmethylcellulose,** b) from about 50 percent to about 20 percent maltodextrin; and c) from about 5 percent to about 10 percent.

CLM What is claimed is:
. . . comprised of, based upon the total dry weight of the subcoating, a) from about 20 percent to about 50 percent **hydroxythylcellulose,** b) from about 45 percent to about 75 percent maltodextrin; and c) from about 1 percent to about 10 percent. . . .

CLM What is claimed is:
18. The dosage form of claim 13, comprising an effective amount of a **pharmaceutical** active ingredient, wherein said dosage form meets USP dissolution requirements for immediate **release** forms of said **pharmaceutical** active ingredient.

CLM What is claimed is:

L57 ANSWER 20 OF 79 USPATFULL on STN (Continued)
23. A **pharmaceutical** dosage form comprising a core and a coating, said coating substantially covering said core, wherein said coating is comprised of. . . .

CLM What is claimed is:
27. The medicament of claim 26 wherein the subcoating comprises materials selected from the group consisting of **cellulose** ethers, plasticizers, polysorbatybrates, pigments, opacifiers, and mixtures thereof.

CLM What is claimed is:
. . . 0.1 percent to about 33 percent of a thickener selected from the group consisting of kappa carrageenan, iota carrageenan, maltodextrin, **gellan gum**, agar, gelling starch, and mixtures thereof; and c) from about 11 percent to about 60 percent of a plasticizer selected. . . .

CLM What is claimed is:
30. A **pharmaceutical** dosage form comprising a core, a subcoating substantially covering said core, and an outer coating substantially covering said subcoating, wherein. . . .

IT Drug delivery systems
(capsules; dip coating compns. containing **cellulose** ethers for capsules and tablets)

IT Plasticizers
(dip coating compns. containing **cellulose** ethers for capsules and tablets)

IT Castor oil

IT Polyoxyalkylenes, biological studies
(dip coating compns. containing **cellulose** ethers for capsules and tablets)

IT Coating process
(dip; dip coating compns. containing **cellulose** ethers for capsules and tablets)

IT Drug delivery systems
(tablets, coated; dip coating compns. containing **cellulose** ethers for capsules and tablets)

IT 7631-86-9, Silica, biological studies
(colloidal; dip coating compns. containing **cellulose** ethers for capsules and tablets)

IT 8050-81-5, Simethicone **9000-07-1**, Carrageenan 9004-62-0, Hydroxyethyl **cellulose** 9004-64-2, Hydroxypropyl **cellulose** 9004-65-3, Hydroxypropyl methyl **cellulose** 11114-20-8, 9049-76-7, Purity Gum 59 9050-36-6, Maltodextrin 11114-20-8, **w**-Carrageenan 11238-66-2, Xanthan gum 25322-68-3, Polyethylene glycol
(dip **coating** compns. containing **cellulose** ethers for capsules and tablets)

IT **9000-07-1**, Carrageenan
(dip **coating** compns. containing **cellulose** ethers for capsules and tablets)

L57 ANSWER 21 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2003:105838 USPATFULL
TITLE: Simethicone as weight gain enhancer
INVENTOR(S): Symoniak, Christopher, Marlton, NJ, UNITED STATES
Gulian, Cynthia, Lansdale, PA, UNITED STATES
Gowan, Walter G., Jr., Woodstock, GA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20030077279	A1	20030417
APPLICATION INFO.:	US 2002-122498	A1	20020415 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2002-122999, filed on 12 Apr 2002, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-29127P	20010515 (60) <--
	US 2001-28732P	20010928 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: AUDLEY A. CIAMPORCERO JR., JOHNSON & JOHNSON, ONE
JOHNSON & JOHNSON PLAZA, NEW BRUNSWICK, NJ, 08933-7003
NUMBER OF CLAIMS: 33
EXEMPLARY CLAIM: 1
LINE COUNT: 1478
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A film forming composition comprised of a film former and a weight gain enhancer selected from simethicone, polysorbate 80 and mixtures thereof, . . .
wherein the weight gain enhancer is used in an amount sufficient to increase the weight gain of the film forming composition on a substrate when dried.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . (OTC) drugs. The ability to combine capsule halves having different colors provided manufacturers with a unique means of distinguishing various **pharmaceutical** products. Many patients prefered capsules over tablets, perceiving them as being easier to swallow. This consumer preference prompted **pharmaceutical** manufacturers to market certain products as capsules, even when they were also available in tablet form. . . .

SUMM . . . alternative to capsule products are caplets, which are solid, oblong tablets that are often coated with various polymers such as **cellulose** ethers to improve their aesthetics, stability, and swallowability. Typically, such polymers are applied to the tablets either from solution in. . . .

SUMM [0007] However, the use of gelatin as a **pharmaceutical** coating material presents certain disadvantages and limitations, including the potential for decreased dissolution rate after extended storage due to cross-linking. . . .

SUMM . . . shells via conventional dip molding processing. See also U.S. Pat. No. 6,001,211 (capsules prepared via pin dip coating with thermogelled **methylcellulose** ether compositions). However, due to potential tampering concerns, hard gelatin capsules are no longer a preferred delivery system for consumer (over-the-counter) **pharmaceutical** dietary supplements, or other such products.

L57 ANSWER 21 OF 79 USPATFULL on STN (Continued)
Additionally, the properties of an ideal composition into which steel pins are to be. . .
SUMM . . . parts water required to dissolve 1 part of the non-polymeric, water soluble solute. See Remington, "The Science and Practice of **Pharmacy**," pages 208-209 (2000). "Water soluble," as used herein in connection with polymeric materials, shall mean that the polymer swells in. . .
SUMM [0017] Dimethicone is a well known **pharmaceutical** material consisting of linear siloxane polymers containing repeating units of the formula [--Si(CH3)2-O--]n and terminated with trimethylsiloxy end blocking units of. . .
SUMM . . . via a dip molding process. One composition comprises, consists of, and/or consists essentially of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and a thickener, such as a hydrocolloid, e.g., xanthan gum or currageenan. In another embodiment, the composition comprises, consists of, and. . . thereof. In another embodiment, the composition comprises, consists of, and/or consists essentially of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; and optionally a plasticizer, such as vegetable oils, e.g., fractionated oil; and may optionally be substantially free of thickeners such. . . gum. In yet another embodiment, the composition comprises, consists of, and/or consists essentially of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, an extender, such as polysorbaydrates, e.g., maltodextrin; and optionally a plasticizer, such as glycols, e.g., polyethylene glycol; polyethers, optionally. . .
SUMM . . . use in film forming composition of the present invention. Examples of suitable film formers include, but are not limited to, **polyvinylalcohol** (PVA), hydroxypropyl starch, hydroxyethyl starch, pullulan, methylethyl starch, carboxymethyl starch, **methylcellulose**, **hydroxypropylcellulose** (HPC), **hydroxyethylmethylcellulose** (HEMC), **hydroxypropylmethylcellulose** (HPMC), **hydroxyethylcellulose** (HEMC), **hydroxyethylethylcellulose** (HEEC), hydroxyethylhydroxypropylmethyl **cellulose** (HEMHPMC), pre-gelatinized starches, and polymers and derivatives and mixtures thereof.
SUMM [0028] One suitable **hydroxypropylmethylcellulose** comprises "HPMC 2910", which is a **cellulose** ether having a degree of substitution of about 1.9 and a hydroxypropyl molar substitution of about 0.23, containing, based upon. . .
SUMM [0029] Any plasticizer known in the **pharmaceutical** art is suitable for use in the present invention, and may include, but not be limited to polyethylene glycol; glycerin, . . . glycol, propylene glycol, dibutyl sebecate, triethyl. . .
SUMM . . . from about 2 percent to about 8 percent, e.g. from about 4 percent to about 6 percent of a water-soluble **cellulose** ether and from about 0.1 percent to about 1 percent, e.g. from about 0.2 percent to about 0.5 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.1 percent to about 1.5 percent, e.g. from about 0.2 percent to about 0.5 percent of a. . .
SUMM . . . to about 90 percent, e.g. from about 80 percent to about 90 percent of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, from about 1 percent to about 80 percent, e.g. from about 5 percent to about 50 percent or from about. . .
SUMM . . . percent to about 15 percent or from about 10 percent to about 14 percent, of a film former such as **hydroxypropylmethylcellulose** and from about 0.05 percent to about 0.2 percent, e.g., from about 0.08 percent to about 0.16 percent or from. . .
SUMM . . . percent to about 30 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**. . .
SUMM . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and is substantially free of hydrocolloids, i.e., e.g. contains less than about 1%, or less than about 0.01% of hydrocolloids.
SUMM . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.001 percent to about 0.1 percent, e.g. from about 0.01 percent to about 0.09 percent of a. . .
SUMM . . . to about 19 percent or from about 16 percent to about 19 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, from about 0.1 percent to about 17 percent, e.g. from about 1 percent to about 15 percent or from about. . .
SUMM . . . opacifying agents such as titanium dioxide, and/or from about 0
percent to about 14 percent colorants. See Remington's Practice of **Pharmacy**, Martin & Cook, 17.esp.th ed., pp. 1625-30, which is herein
incorporated by reference.
SUMM [0044] Any coloring agent suitable for use in **pharmaceutical** applications may be used in the present invention and may include, but not be limited to azo dyes, quinophthalone dyes, . . .

L57 ANSWER 21 OF 79 USPATFULL on STN (Continued)
SUMM [0046] In one embodiment, the **pharmaceutical** dosage form is comprised of a) a core containing an active ingredient; b) an optional first coating layer comprised of. . .
SUMM . . . and 6,274,162, which are all incorporated by reference herein. Additional suitable subcoatings include one or more of the following ingredients: **cellulose** ethers such as **hydroxypropylmethylcellulose**, **hydroxypropylcellulose**, and **hydroxyethylcellulose**; polysaccharides such as xanthan gum, starch, and maltodextrin; plasticizers including for example, glycerin, polyethylene glycol, propylene glycol, dibutyl sebecate, triethyl. . .
SUMM . . . from about 5 percent to about 8 percent, e.g. from about 4 percent to about 6 percent of a water-soluble **cellulose** ether and from about 0.1 percent to about 1 percent, e.g. from about 0.2 percent to about 0.5 percent, of a film former such as a **cellulose** ether, e.g.,

L57 ANSWER 21 OF 79 USPATFULL on STN (Continued)
hydroxypropylmethylcellulose, and from about 0.1 percent to about 1.5 percent of a thickener such as a hydrocolloid, e.g., xanthan gum. . .
SUMM . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**. . .
SUMM . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and is substantially free of hydrocolloids, i.e., e.g. contains less than about 1%, or less than about 0.01% of hydrocolloids.
SUMM . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.1 percent to about 1.0 percent, e.g. from about 0.25 percent to about 0.5 percent of a. . .
SUMM . . . to about 90 percent, or from about 80 percent to about 90 percent of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, from about 1 percent to about 80 percent, e.g. from about 5 percent to about 50 percent or from about. . .
SUMM . . . percent to about 15 percent or from about 10 percent to about 14 percent, of a film former such as **hydroxypropylmethylcellulose** and from about 0.05 percent to about 0.2 percent, e.g., from about 0.08 percent to about 0.16 percent or from. . .
SUMM . . . percent to about 30 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**. . .
SUMM . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and is substantially free of hydrocolloids, i.e., e.g. contains less than about 1%, or less than about 0.01% of hydrocolloids.
SUMM . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.001 percent to about 0.1 percent, e.g. from about 0.01 percent to about 0.09 percent of a. . .
SUMM . . . to about 19 percent or from about 16 percent to about 19 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, from about 0.1 percent to about 17 percent, e.g. from about 1 percent to about 15 percent or from about. . .
SUMM . . . opacifying agents such as titanium dioxide, and/or from about 0
percent to about 14 percent colorants. See Remington's Practice of **Pharmacy**, Martin & Cook, 17.esp.th ed., pp. 1625-30, which is herein
incorporated by reference.
SUMM [0044] Any coloring agent suitable for use in **pharmaceutical** applications may be used in the present invention and may include, but not be limited to azo dyes, quinophthalone dyes, . . .

L57 ANSWER 21 OF 79 USPATFULL on STN (Continued)
SUMM [0046] In one embodiment, the **pharmaceutical** dosage form is comprised of a) a core containing an active ingredient; b) an optional first coating layer comprised of. . .
SUMM . . . and 6,274,162, which are all incorporated by reference herein. Additional suitable subcoatings include one or more of the following ingredients: **cellulose** ethers such as **hydroxypropylmethylcellulose**, **hydroxypropylcellulose**, and **hydroxyethylcellulose**; polysaccharides such as xanthan gum, starch, and maltodextrin; plasticizers including for example, glycerin, polyethylene glycol, propylene glycol, dibutyl sebecate, triethyl. . .
SUMM . . . from about 5 percent to about 8 percent, e.g. from about 4 percent to about 6 percent of a water-soluble **cellulose** ether and from about 0.1 percent to about 1 percent, e.g. from about 0.2 percent to about 0.5 percent, of a film former such as a **cellulose** ether, e.g.,

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hydroxypropylmethylcellulose, and from about 0.1 percent to about 1.5 percent of a thickener such as a hydrocolloid, e.g., xanthan gum. . .
SUMM . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**. . .
SUMM . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and is substantially free of hydrocolloids, i.e., e.g. contains less than about 1%, or less than about 0.01% of hydrocolloids.
SUMM . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.1 percent to about 1.0 percent, e.g. from about 0.25 percent to about 0.5 percent of a. . .
SUMM . . . to about 90 percent, or from about 80 percent to about 90 percent of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, from about 1 percent to about 80 percent, e.g. from about 5 percent to about 50 percent or from about. . .
SUMM . . . percent to about 15 percent or from about 10 percent to about 14 percent, of a film former such as **hydroxypropylmethylcellulose** and from about 0.05 percent to about 0.2 percent, e.g., from about 0.08 percent to about 0.16 percent or from. . .
SUMM . . . percent to about 30 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**. . .
SUMM . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and is substantially free of hydrocolloids, i.e., e.g. contains less than about 1%, or less than about 0.01% of hydrocolloids.
SUMM . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.001 percent to about 0.1 percent, e.g. from about 0.01 percent to about 0.09 percent of a. . .
SUMM . . . to about 19 percent or from about 16 percent to about 19 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, from about 0.1 percent to about 17 percent, e.g. from about 1 percent to about 15 percent or from about. . .
SUMM . . . opacifying agents such as titanium dioxide, and/or from about 0
percent to about 14 percent colorants. See Remington's Practice of **Pharmacy**, Martin & Cook, 17.esp.th ed., pp. 1625-30, which is herein
incorporated by reference.
SUMM [0044] Any coloring agent suitable for use in **pharmaceutical** applications may be used in the present invention and may include, but not be limited to azo dyes, quinophthalone dyes, . . .

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gelatin-containing compositions. Thicke. . . .

DETD . . .	212.3	566.67	566.67	566.67	566.67
Maltodextrin	0	53	53	67	67
PEG 400	0	7	7	5	5
Hydroxy-	0	0	0	0	0
ethylcellulose*					
Total coating solution	233.3	666.67	666.67	666.67	666.67
Wt % solids in coating solution	9%	15%	15	15	15

*Available from Aqualon, under the tradename, "Natrosol. . . .

DETD . . . oil	0	0	0	0.13
HPMC (1910, 5 mPas)	0	0	0	32.4
PEG 400	5	5	0	
Hydroxy-	24	24	0	
ethylcellulose*				
Total coating solution	666.67	666.67	722.9	
Wt % solids in coating solution	15%	15%	4.5%	

*Available from Aqualon, under the tradename,
DETD [0126] 88.4 kg (9% w/w) of hydroxypropyl **methylcellulose** 2910, 5 mPa and 0.347 kg (0.04% w/w) of castor Oil were mixed into 593.8 kg (91% w/w) of purified.
DETD Preparation of Tablets Dip **Coated** with HPMC/**Carrageenan** Dipping Solutions
CLM What is claimed is:
. . . 2. The film forming composition of claim 1 wherein the film former is selected from the group consisting of **polyvinylalcohol**, hydroxypropyl starch, hydroxyethyl starch, pullulan, methylethyl starch, carboxymethyl
starch, **methylcellulose**, **hydroxypropylcellulose**, **hydroxypropylmethylcellulose**, **hydroxypropylmethylcellulose**, **hydroxyethylcellulose**, hydroxyethylhydroxypropylmethyl **cellulose**, pre-gelatinized starches, and polymers and derivatives and mixtures thereof.
CLM What is claimed is:
. . . 4. The film forming composition of claim 2 wherein the hydrocolloid is a gum and the film former is a **cellulose** ether.
CLM What is claimed is:
. . . 7. The film forming composition of claim 2 wherein the hydrocolloid is xanthan gum and the film former is hydroxypropylmethyl **cellulose**.
CLM What is claimed is:
. . . based upon the total weight of the composition, a) from about 60 percent to about 99.9 percent of a hydroxypropylmethyl **cellulose** film former; b) from about 0.5 percent to about 5 percent of a xanthan gum hydrocolloid; and c) from about. . .
CLM What is claimed is:
. . . based upon the total weight of the composition, a) from about 85 percent to about 99.5 percent of a hydroxypropylmethyl **cellulose** film

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former; and b) from about 0.5 percent to about 5 percent of a xanthan gum hydrocolloid; and c) from. . .
CLM What is claimed is:
14. A dosage form for delivering **pharmaceuticals**, nutritionals, nutraceuticals, vitamins, minerals, supplements, flavoring agents or mixtures thereof comprising an outer coating, said outer coating comprised of the. . .
CLM What is claimed is:
15. A **pharmaceutical** dosage form comprising an outer coating of the composition of claim 9.
. . .
CLM What is claimed is:
16. A **pharmaceutical** dosage form comprising a core, a subcoating substantially covering said core, and an outer coating substantially covering said subcoating, wherein. . .
CLM What is claimed is:
17. The dosage form of claim 16 wherein the subcoating is selected from the group consisting of: **hydroxypropylmethylcellulose**, **hydroxypropylcellulose**, **hydroxyethylcellulose**, xanthan gum, starch, maltodextrin, dextrin, polyethylene glycol, propylene glycol, dibutyl sebecate, triethyl citrate, castor oil, polysorbate-80, sodium lauryl sulfate, dicetyl-sodium. . .
CLM What is claimed is:
. comprised of, based upon the total dry weight of the subcoating, a) from about 2 percent to about 8 percent **hydroxypropylmethylcellulose**; and b) from about 0.1 percent to about 1 percent castor oil.
. . .
CLM What is claimed is:
. . . comprised of, based upon the total dry weight of the subcoating, a) from about 20 percent to about 50 percent **hydroxypropylmethylcellulose**; b) from about 45 percent to about 75 percent maltodextrin; c) from about 1 percent to about 10 percent PEG. . . .
CLM What is claimed is:
. . . comprised of, based upon the total dry weight of the subcoating, a) from about 25 percent to about 40 percent **hydroxyethylcellulose**; b) from about 50 percent to about 70 percent maltodextrin; c) from about 5
percent to about 10 percent PEG. . .
CLM What is claimed is:
22. The dosage form of claim 15 further comprising an effective amount of a **pharmaceutical** active ingredient, wherein said dosage form meets USP dissolution requirements for immediate **release** forms of said **pharmaceutical** active ingredient.
. . .
CLM What is claimed is:
25. A **pharmaceutical** dosage form comprising a core and a coating; said coating substantially covering said core and having a surface gloss
of. . .
CLM What is claimed is:
29. The medicament of claim 28 wherein the subcoating comprises materials selected from the group consisting of **cellulose** ethers, plasticizers, polyoxalkylates, pigments, opacifiers, and mixtures

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ACCESSION NUMBER: 2003:152893 USPATFULL
TITLE: Dip coating compositions containing **cellulose** ethers
INVENTOR(S): Gillan, Cynthia, Lansdale, PA, UNITED STATES
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	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003070084	A1	20030417
APPLICATION INFO.:	US 2002-122999	A1	20020412 (10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-291127P	20010515 (60)	<--
	US 2001-327749P	20010928 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: AUDLEY A. CIAMPORCERO JR., JOHNSON & JOHNSON, ONE
JOHNSON & JOHNSON
PLAZA, NEW BRUNSWICK, NJ, 08933-7003
NUMBER OF CLAIMS: 40
EXEMPLARY CLAIM: 1
LINE COUNT: 1493
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Water soluble, gelatin-free dip coatings for **pharmaceutical** solid dosage forms such as tablets comprising HPMC and xanthan gum, carrageenan, and mixtures thereof, or HPMC and castor oil or maltodextrin.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Dip coating compositions containing **cellulose** ethers

AB Water soluble, gelatin-free dip coatings for **pharmaceutical** solid dosage forms such as tablets comprising HPMC and xanthan gum, carrageenan, and mixtures thereof, or HPMC and castor oil. . .
SUM . . . (6072) drugs. The ability to combine capsule halves having different colors provides manufacturers with a unique means of distinguishing various **pharmaceutical** products. Many patients preferred capsules over tablets, perceiving them as being easier to swallow. This consumer preference prompted **pharmaceutical** manufacturers to market certain products in capsule form even when they were also available in tablet form.
SUM . . . alternatives to capsule products are caplets, which are solid, oblong tablets that are often coated with various polymers such as **cellulose** ethers to improve their aesthetics, stability, and swallowability. Typically, such polymers are applied to the tablets either from solution in. . .
SUM [0007] However, the use of gelatin as a **pharmaceutical** coating material presents certain disadvantages and limitations, including the potential for decreased dissolution rate after extended storage due to cross-linking. . .
SUM . . . shells via conventional dip molding processing. See also U.S. Pat. No. 6,90[23] (capsules prepared via pin dip coating with

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thereof. . .
TT 50-70-4, Sorbitol, biological studies 56-81-5, Glycerol, biological studies 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 57-55-6, 1,2-Propylene glycol, biological studies 77-93-0, Triethyl citrate 79-94-7, Tributyl citrate 102-76-1, Glycerol triacetate 109-43-3, Dibutyl sebacate 151-21-3, Sodium lauryl sulfate, biological studies 577-11-7, Sodium dioctylsulfosuccinate 1332-37-2, Iron oxide, biological studies 1398-61-4, Chitin 9004-81-5, Dimethicone 9000-01-5, Gum arabic 9000-07-1, Carrageenan 9000-30-0, Guar gum 9000-40-2, Locust bean
gum 9000-65-1, Tragacanth gum 9000-69-5, Pectin 9002-18-0, Agar 9002-89-5, Polyvinylalcohol 9004-34-6, Cellulose, microcrystalline 9004-57-4, Ethyl cellulose 9005-27-0, Hydroxyethyl starch 9005-32-7, Alginic acid 9005-65-6, Polysorbate 80 9005-70-5, Inulin 9008-22-4, Lysozyme 9012-76-4, Chitosan 9032-42-2, Hydroxyethyl methyl cellulose 9041-56-9, Hydroxypropyl methyl cellulose 9049-76-7, Hydroxypropyl starch 9050-36-6, Maltodextrin 9057-02-7, Pullulan 9057-04-1, Carboxymethyl starch 11078-30-1, Galactomannan 11113-66-9, Iron hydroxide 11138-66-2, Xanthan gum 12619-70-4, Cyclodextrin 13463-67-7, Titanium
dioxide, biological studies 25395-31-7, Glyceryl diacetate 26446-35-5, Glyceryl monoacetate 37231-28-5, Pullulan 39300-88-4, Tara gum 39464-87-4, Sclerotiglucan 55819-15-3, Hydroxyethyl hydroxypropyl methyl cellulose **71010-52-1**, **Gellan gum** 74749-76-1, Zooglan 77323-57-0, Methyl ethyl starch 85581-59-8, Methylan 96949-23-2, Rhamsan gum 96949-22-3, Welan gum (dimethicone as weight gain enhancer)
IT **71010-52-1**, **Gellan gum**
(dimethicone as weight gain enhancer)

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(hemoglelated **methylcellulose** ether compositions). However, due to potential tampering concerns, hard gelatin capsules are no longer a preferred delivery system for consumer over-the-counter **pharmaceuticals**, dietary supplements, or other such products. Additionally, the properties of an ideal composition into which steel pins are to be. . .
SUM04 [0011] a) hydroxypropylmethyl **cellulose**; and
SUM04 [0013] a) hydroxypropylmethyl **cellulose**; and
SUM04 [0019] a) hydroxypropylmethyl **cellulose**; and
SUM04 . . . parts water required to dissolve 1 part of the non-polyelectric, water soluble solute. See Remington, "The Science and Practice of **Pharmacy**," pages 208-209 (2000). "Water soluble," as used herein in connection with polymeric materials, shall mean that the polymer swells in.
SUM04 [0024] Dimethicone is a well known **pharmaceutical** material consisting of linear siloxane polymers containing repeating units of the formula [--(CH.sub.2).sub.2Si(O).sub.2SiO]n stabilized by trimethylsilyl end blocking units of.
SUM04 . . . via a dip molding process. One composition comprises, consists of, and/or consists essentially of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; and a thickener, such as a hydrocolloid, e.g., xanthan gum or carrageenan. In another embodiment, the composition comprises, consists of, and. . . thereof. In yet another embodiment, the composition comprises, consists of, and/or consists essentially of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and optionally a plasticizer, such as vegetable oils, e.g., castor oil, and optionally be substantially free of thickeners such. . . gum. In yet another embodiment, the composition comprises, consists of, and/or consists essentially of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose** (HPMC), an extender, such as polyacrylodrates, e.g. maltodextrin; and optionally a plasticizer, such as glycols, e.g., polyethylene glycol; and say optionally. . .
SUM04 . . . use in film forming composition of the present invention. Examples of suitable film formers include, but are not limited to, **polyvinylalcohol** (PVA), hydroxypropyl starch, hydroxyethyl starch, pullulan, methylethyl starch, carboxymethyl starch, **methylcellulose**, **hydroxypropylcellulose** (HPC), **hydroxyethylmethylcellulose** (HEMC), **hydroxypropylmethylcellulose** (HPMC), hydroxybutylmethylcellulose (HBMC), **hydroxyethylcellulose** (HEC), hydroxyethylhydroxypropylmethyl **cellulose** (HEHPMC), pre-gelatinized starches, and polymers and derivatives and mixtures thereof.
SUM04 [0027] One suitable **hydroxypropylmethylcellulose** compound is 'HPMC 2910', which is a **cellulose** ether having a degree of substitution of about 1.9 and a hydroxypropyl molar substitution of 0.23, and containing, based upon
SUM04 [0032] Any plasticizer known in the **pharmaceutical** art is suitable for use in the present invention, and may include, but not be limited to polyethylene glycol; glycerin. . . glycol; mono acetate of glycerol;
diacetate of glycerol; triacetate of glycerol; natural gums and mixtures
thereof. In solutions containing a **cellulose** ether film former, an optional plasticizer may be present in an amount, based upon the total weight of the solution, . . .
SUM04 [0035] In embodiments wherein a **cellulose** ether film former is used in the composition, the film forming composition for dip coating substrates

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SUMM may be substantially free . . . than about 100 percent, e.g. from about 95 percent to about 99.5 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.5 percent to about 5 percent of a thickener such as a hydrocolloid, e.g., xanthan gum. . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**.

SUMM . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and substantially free of hydrocolloid, i.e., contains less than about 1%, or less than about 0.01% of hydrocolloids.

SUMM . . . to about 100 percent, e.g. from about 97 percent to about 100 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and from about 0.1 percent to about 1.0 percent, e.g. from about 0.25 percent to about 0.5 percent of a. . .

SUMM . . . to about 90 percent, or from about 80 percent to about 90 percent of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; from about 1 percent to about 90 percent, e.g. from about 5 percent to about 50 percent or from about.

SUMM . . . percent to about 15 percent or from about 10 percent to about 14 percent, of a film former such as **hydroxypropylmethylcellulose** and from about 0.05 percent to about 0.2 percent, e.g. from about 0.08 percent to about 0.18 percent or from.

SUMM . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**.

SUMM . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**, and is substantially free of hydrocolloids, i.e., e.g. contains less than about 1%, or less than about 0.01% of hydrocolloids.

SUMM . . . percent to about 20 percent or from about 10 to about 16 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; and from about 0.001 percent to about 0.1 percent, e.g. from about 0.01 percent to about 0.09 percent of a. . .

SUMM . . . to about 19 percent or from about 18 percent to about 19 percent, of a film former such as a **cellulose** ether, e.g., **hydroxypropylmethylcellulose**; from about 0.1 percent to about 17 percent, e.g. from about 1 percent to about 11 percent or from about.

SUMM . . . opacifying agents such as titanium dioxide, and/or from about 0 . . . percent to about 14 percent colorants. See Remington's Practice of **Pharmacy**, Martin & Cook, 17th ed., pp. 1625-35, which is herein incorporated by reference.

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shelf-life and storage period at elevated temperature and humidity conditions. In particular, these **cellulose**-ether based compositions according to the present invention were also advantageously more resistant to microbial growth, which thereby enabled a longer. other dipping dispersions of the present invention may have been higher than that typically found in gelatin-based dipping solutions, the **cellulose**-ether based compositions of the present invention surprisingly required a shorter drying cycle time relative to that for gelatin-containing compositions. Third, ...

DETD . . . 212.3	566.67	566.67	566.67	566.67
maltodextrin 0	53	53	67	67
PEG 400 0	7	7	5	5
Hydroxy- **ethylcellulose**' 0	0	0	0	0
Total coating solution	233.3	666.67	666.67	666.67	666.67
Wt % solids in coating solution	9%	15%	15	15	15

*Available from Aqualon, under the tradename, "Natrosol. . .

DETD	0	0	0.13
HPMC (1910,	0	0	32.4
5 nPas)			
PEG 400	5	5	0
Hydroxy- **ethylcellulose**'	24	24	0
Total coating solution	666.67	666.67	722.9
Wt % solids in coating solution	15%	15%	4.5%

*Available from Aqualon, under the tradename,

DETD [0148] 88.4 kg (9% w/w) of hydroxypropyl **methylcellulose** 2910, 5 nPs and 0.347 kg (0.3% w/w) of castor Oil were mixed into 593.8 kg (91% w/w) of purified.

DETD [0162] Preparation of Tablets Dip **Coated** with HPMC/**Carrageenan** Dipping Solutions

CLM What is claimed is:

1. A water soluble composition for dip-coating a substrate comprised of:

a) hydroxypropylmethyl **cellulose**; and b) a thickener selected from the group consisting of xanthan gum, carrageenan, and mixtures thereof, wherein the composition possesses. . .

CLM What is claimed is:

. . . the total dry weight of the composition, a) from about 95 percent to . . . less than about 100 percent of hydroxypropylmethyl **cellulose**; and b) from about 0.5 percent to about 5 percent of a thickener selected from the group consisting of xanthan. . .

CLM What is claimed is:

. . . based upon the total dry weight of the composition, a) from about 95 . . . percent to about 99.5 percent of hydroxypropylmethyl **cellulose**; and b) from about 0.5 percent to about 5 percent of xanthan gum.

CLM What is claimed is:

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SUMM [0051] Any coloring agent suitable for use in **pharmaceutical** applications may be used in the present invention and may include, but not be limited to azo dyes, quinophalene dyes,

SUMM [0053] In one embodiment, the **pharmaceutical** dosage form is comprised of a) a core containing an active ingredient; b) an optional first coating layer comprised of. . . .

SUMM . . . and 6,274,162, which are all incorporated by reference herein. Additional suitable substances include one or more of the following ingredients: **cellulose** ethers such as **hydroxypropylmethylcellulose**, **hydroxypropylcellulose**, and hydroxypropyl; polysaccharides such as xanthan gum, starch, and maltodextrin; plasticizers including for example, glycerin, polyethylene glycol, propylene glycol, dibutyl; sebecate, triethyl.

SUMM . . . from about 2 percent to about 8 percent, e.g. from about 4 percent to about 6 percent of a water-soluble **cellulose** ether and from about 0.1 percent to about 1 percent, castor oil, as disclosed in detail . . . in U.S. Pat. No. . . .

SUMM [0060] In one embodiment, the film former is a **cellulose** ether such as HPMC, and the thickener is a hydrocolloid such as xanthan gum and the weight gain enhancer is. . . .

SUMM . . . any material that can be carried by or entrained in the system.

For example, the active agent can be a **pharmaceutical**, nutraceutical, vitamin, dietary supplement, nutrient, herb, foodstuff, dyestuff, nutritional, mineral, supplement, or flavoring agent or the like and combinations thereof.

SUMM . . . . methenamine mandelate; menthol; meperidine hydrochloride; metaproterenol sulfate; methaqualomine and its nitrates; methergide and its maleate; methyl nicotinate; methyl salicylate; methyl **cellulose**; methsuximide; metoclopramide and its halides/hydrates; mitoxindiella; metoprotol tartrate; miconazole nitrate; mineral oil; minoxtil; morphine; naproxen and its alkali metal sodium. . . . of active drug or a suspension trisilicate base and on a magnesium aluminum

silicate base, and mixtures thereof. Mixtures and **pharmaceutically** acceptable salts of these and other actives can be used.

SUMM [0067] In one embodiment, the dosage form (with the dip coatings of the present invention provided for immediate **release** of the active ingredient, i.e. the dissolution of the dosage form conformed to USP specifications for immediate **release** tablets containing the particular active ingredient employed. For example, for acetaminophen tablets, . . .

U.S. Pat. No. 24 specifies that in pH. . . . using USP apparatus 2 (paddles)

at 50 rpm, at least 80% of the acetaminophen contained in the dosage form is **released** therefrom within 30 minutes after dosing, and for ibuprofen tablets, U.S. Pat. No. 24 specifies that in pH 7.2 phosphate. . . . using USP apparatus 2 (paddles) at 50 rpm, at least 80% of the ibuprofen contained in the dosage form is released therefrom within 60 minutes after dosing. See U.S. Pat. No. 24, 2000 Version, 19-20 and 856 (1999).

SUMM . . . retained acceptable dissolution characteristics for the desired

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10. A **pharmaceutical** dosage form comprising an outer coating of the composition of claim 2.

CLM What is claimed is:

11. A **pharmaceutical** dosage form comprising a core, a subcoating substantially covering said core, and an outer coating substantially covering said subcoating, wherein.

CLM What is claimed is:

12. The coated dosage form of claim 11 wherein the subcoating comprises materials selected from the group consisting of **Cellulose** ethers, plasticizers, polycarbohydrates, pigments, opacifiers, and mixtures thereof.

CLM What is claimed is:

13. The coated dosage form of claim 11 wherein the subcoating comprises materials selected from the group consisting of **hydroxypropylmethylcellulose**, castor oil, polyethylene glycol, polysorbate 80, maltodextrin, and mixtures thereof.

CLM What is claimed is:

. . . upon the total dry weight of the subcoating, a) from about 2 percent

to about 8 percent of a water-soluble **cellulose** ether selected from the group consisting of **hydroxypropylmethylcellulose**, **hydroxypropylcellulose**, **hydroxyethylcellulose**, and mixtures thereof. b) from about 0.1 percent to about 1 percent castor oil.

CLM What is claimed is:

. . . comprised of, based upon the total dry weight of the subcoating, a) from about 4 percent to about 6 percent **hydroxypropylmethylcellulose**; and b) from about 0.1 percent to about 1 percent castor oil.

CLM What is claimed is:

16. The dosage form of claim 15 wherein the **hydroxypropylmethylcellulose** has a viscosity of about 5000 cps in an aqueous solution containing 2 weight percent **hydroxypropylmethylcellulose**.

CLM What is claimed is:

17. The dosage form of claim 11 wherein the subcoating is comprised of, based upon the total dry weight of the subcoating, a) from about 20 percent to about 50 percent **hydroxypropylmethylcellulose**; b) from about 45 percent to about 75 percent maltodextrin; c) from about 1 percent to about 10 percent PEG. . . .

CLM What is claimed is:

. . . comprised of, based upon the total dry weight of the subcoating, a) from about 25 percent to about 40 percent **hydroxyethylcellulose**, b) from about 50 percent to about 70 percent maltodextrin; c) from about 5

percent to about 10 percent PEG. . . .

CLM What is claimed is:

20. The coated dosage form of claim 11, further comprising an effective amount of a **pharmaceutical** active ingredient, wherein said dosage form meets USP dissolution requirements for immediate **release** forms of said **pharmaceutical** active ingredient.

CLM What is claimed is:

. . . of, based upon the total weight of the aqueous dispersion, a) from

L57 ANSWER 22 OF 79 USPATFULL on STN (Continued)
about 10 percent to about 14 percent of **hydroxypropylmethylcellulose**; and b) from about 0.2 percent to about 0.34 percent of xanthan gum.

CLM What is claimed is:
25. A **pharmaceutical** dosage form comprising a core and a coating, said coating substantially covering said core and having a surface gloss of.

CLM What is claimed is:
. . . total dry weight of the coating composition, a) from about 95 percent to less than about 100 percent of hydroxypropylmethyl **cellulose**; and b) from about 0.5 percent to about 5 percent of xanthan gum.

CLM What is claimed is:
90. The medicament of claim 29 wherein the subcoating comprises materials selected from the group consisting of **cellulose** ethers, plasticizers, polysaccharydrates, pigments, opacifiers, and mixtures thereof.

CLM What is claimed is:
31. A water soluble composition for dip-coating a substrate comprised of: a) hydroxypropylmethyl **cellulose**; and b) castor oil, wherein the composition possesses a surface gloss of at least 150 when applied via dip coating. . .

CLM What is claimed is:
32. A **pharmaceutical** dosage form comprising a core and a coating, said coating substantially covering said core; wherein said coating comprises:
the composition. . .

CLM What is claimed is:
34. A water soluble composition for dip-coating a substrate comprised of: a) hydroxypropylmethyl **cellulose**; and b) maltodextrin, wherein the composition possesses a surface gloss of at least 150 when applied via dip coating to. . .

CLM What is claimed is:
36. A **pharmaceutical** dosage form comprising a core and a coating, said coating substantially covering said core; wherein said coating comprises:
the composition. . .

CLM What is claimed is:
. . . total dry weight of the composition: a) greater than about 95 percent and less than about 99.5 percent of hydroxypropylmethyl **cellulose**; and b) greater than about 0.5 percent and less than about 5 percent of carrageenan, wherein the composition possesses a. . .

CLM What is claimed is:
39. A **pharmaceutical** dosage form comprising a core and a coating, said coating substantially covering said core; wherein said coating comprises the composition. . .

IT Drug delivery systems
(capsules; dip coating compns. containing **cellulose** ethers for capsules and tablets)

IT Plasticizers
(dip coating compns. containing **cellulose** ethers for capsules and tablets)

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TITLE: Edible coating composition
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NUMBER OF CLAIMS: 46
EXEMPLARY CLAIM: 1
LINE COUNT: 1521
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable **coating** composition containing microcrystalline **cellulose** and **carrageenan** and either a strengthening polymer, a plasticizer or both. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

SUMM [0002] This invention relates to edible, hardenable, prompt **release** **coating** compositions comprising microcrystalline **cellulose**, **carrageenan** and at least one of a strengthening polymer or a plasticizer. The coatings of the present invention can be applied to **pharmaceutical**, including nutraceutical, and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets
and granules, and foods; are readily. . . media, and, when applied
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IT Castor oil
IT Polyoxyalkylenes, biological studies
(dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT Coating process
(dip; dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT Drug delivery systems
(tablets, coated; dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT 7631-86-9, Silica, biological studies
(colloidal; dip coating compns. containing **cellulose** ethers for capsules and tablets)
IT 8050-81-5, Dimethicone **9000-07-1**, Carrageenan 9004-62-0, Hydroxyethyl **cellulose** 9064-64-2, Hydroxypropyl **cellulose** 9004-65-3, Hydroxypropyl methyl **cellulose** 9049-76-7, Purity Gum 59 9050-36-6, Maltodextrin 11114-20-8, κ-Carrageenan 11138-66-2, Xanthan gum 25322-68-3, Polyethylene glycol
(dip **coating** compns. containing **cellulose** ethers for capsules and tablets)
IT **9000-07-1**, Carrageenan
(dip **coating** compns. containing **cellulose** ethers for capsules and tablets)

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. a coating and ingested by, for example, a human, do not significantly retard or extend **release** of active ingredient(s) from a substrate coated therewith.

SUMM [0003] It is a common practice to coat **pharmaceutical** and veterinary tablets to obtain several advantages. Among these are to mask unpleasant
tasting active ingredients with a barrier coat, . .

SUMM [0004] Another very important function of a **pharmaceutical** or veterinary tablet coating is to improve the integrity of the tablet itself. Uncoated tablets are often subject to being. . .

SUMM [0010] Currently, most commercially available edible coatings utilize a synthetic **cellulosic** polymer such as **hydroxypropylmethylcellulose** (HPMC). Other synthetic film-formers which are commonly used include **ethylcellulose**, **methylcellulose**, **polyvinylpyrrolidone**, and polydextrose. These coating materials may be used alone or in combination with secondary film-formers such as sodium alginate or. . .

SUMM . . . proportion to the increase in disintegration time. Many other agents commonly used in coating compositions are also known to delay **release** of **pharmaceutical** agents, such as enteric coatings which use polymeric film forming materials which are insoluble in water, or gastric fluid, some of these being specifically selected to by-pass both
the stomach and small intestine and provide colonic **release**.

SUMM [0013] The coatings of this invention meet U.S. **Pharmacopeia** standards for rapid or immediate dissolution (U.S.P., monograph 23) of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates. Thus, they do not adversely impact or retard **release** of active ingredients from a substrate coated with them. Further, the coatings of this invention are readily dispersed and rapidly. . .

SUMM . . . with the present invention by a coating composition which comprises a unique combination of materials specifically adapted for a prompt **release** when placed aqueous media or ingested, e.g., by a human. The coating composition of the present invention comprises microcrystalline **cellulose**, carrageenan, and at least one of a strengthening polymer and a plasticizer. More specifically, the present invention provides a prompt **release**, edible, hardenable **coating** composition comprising microcrystalline **cellulose** and **carrageenan**, and at least one of strengthening polymer or plasticizer, preferably both, as well as to dry coatings and aqueous dispersions.

SUMM [0015] The present invention also provides **pharmaceutical**, including nutraceutical, and veterinary solid dosage forms, confectionery, seeds,
animal feed, fertilizers, pesticide tablets and granules, and foods coated with the prompt **release** edible, hardenable composition of this invention.

SUMM . . . application, the term "edible" is intended to mean food grade materials which are approved by regulatory authorities for use in **pharmaceutical** or food applications. The term "hardenable" used to describe the coating compositions of this invention is intended to include only. . . that can be handled and packaged but which do not resist abrasive forces significantly. The terms "immediate", "rapid" or "prompt" **release** as applied to dissolution rates or times for the coating compositions of this invention or tablets coated with the compositions of this invention means that the coatings of this
invention

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meet U.S. **Pharmacopoeia** standards (U.S.P. monograph 23) for rapid or immediate dissolution of active ingredients from tablets or other solid dosage forms coated thereon. The, they provide prompt release or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrate. They do not, consistent with the **pharmacopeia** standards above, when placed in aqueous media or ingested by, e.g., a human, significantly impact or retard **release** or dissolution of tablets or other solid dosage forms coated therewith. For example, coatings made in accordance with the present . . . completely disintegrated and/or dissolved within not less than 16 minutes after being ingested or placed in aqueous media. Thus, when a **pharmaceutical** is ingested or placed in the body the coating of this invention and ingested by a human or other animal, the . . .
SUMM [0017] The microcrystalline **cellulose**, which is combined with carrageenan or simply blended therewith, interacts with the carrageenan to provide important functional properties not imparted to provide an
SUMM [0018] Microcrystalline **cellulose** is a purified, partially depolymerized **cellulose** that is generally produced by treating a source of **cellulose**, preferably alpha **cellulose**, in the form of pulp from fibrous plants, with a mineral acid, preferably hydrochloric acid. The acid selectively attacks the less ordered regions of the **cellulose** polymer chain, thereby exposing and freeing the crystallite sites, forming the crystalline aggregates which are known as microcrystalline **cellulose**. These are then separated from the reaction mixture and washed to remove degraded by-products. The resulting wet mass, generally containing 40 to 60 percent moisture, is referred to in the art by several names, including hydrolyzed **cellulose**, microcrystalline **cellulose**, microcrystalline **cellulose** wetcake, or simply wetcake. This microcrystalline **cellulose** wetcake may be used as such or may be further modified, for example, by attrition and/or drying, and utilized in . . .
SUMM [0019] Microcrystalline **cellulose** may also be produced for use in the present invention using a process similar to treatment. In this process, wood chips or other **cellulosic** materials are placed in a chamber into which super-heated steam is introduced. The steam is allowed for a period of about 1-5 minutes, the exit valve is opened rapidly, releasing the contents and explosively yielding microcrystalline **cellulose**. No additional acid need be introduced into the reaction mixture, since it is believed that the acidic materials in the wood chips and the elevated temperature and pressure hydrolyze the **cellulose** and degrade it. In addition to the specific forms of microcrystalline **cellulose**, the present invention also contemplates the use of other **cellulose** derivatives, including microcrystalline **cellulose**, also known as microcrystalline microcrystalline **cellulose**, and powdered **cellulose** such as a commercial material sold as "Solka Floc®."
SUMM [0020] As discussed in greater detail below, the microcrystalline **cellulose** preferred for use in the present invention is microcrystalline **cellulose** which has an average particle size below

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about 100 microns, preferably microcrystalline **cellulose** which been attrited or has an average particle size in the range of 1 to 50 microns, preferably 1 to . . .
SUMM [0023] Carrageenan is used in combination with microcrystalline **cellulose** to form the elegant prompt **release** coatings of the present invention. **Carrageenan** for use in the present invention is a naturally derived carrageenan, including the grades further defined below as iota, kappa, . . . sulfate content of iota carrageenan may range from about 25% to 34%, preferably about 32%. This is intermediate between kappa **carrageenan** which has a 25% sulfate content and lambda carrageenan which has a 35% ester sulfate content. The sodium salt of iota carrageenan is . . . carrageenan requires heating water to different temperatures to dissolve them. The iota carrageenan which are suitable for the microcrystalline **cellulose**/iota carrageenan material of this invention are soluble in water heated up to 50° C. (176° F.). Preferred grades of iota . . .
STMM [0027] The microcrystalline **cellulose** and carrageenan may be coprocessed as may be blended in any suitable manner, such as dry blending.
STMM [0028] Coprocessed microcrystalline **cellulose**/iota carrageenan is rapidly peptizable. Peptization means that the dry agent can readily be dispersed in water in a colloidal state. . . . be dispersed (peptized)
in a colloidal state with minimal agitation. Thus, the novel coating formulations in which the coprocessed microcrystalline **cellulose**/iota carrageenan is incorporated can be hydrated in as little as 0.5 hour, but more preferably require 1 to 3 hours. . . .
SUMM [0029] The coprocessed microcrystalline/iota carrageenan compositions useful in this invention may be prepared by first stirring hydrolyzed **cellulose** wetcake, such that the average particle size of the wetcake particles is generally not more than about 20 microns, preferably. . . .
at which the particular grade of iota carrageenan being used dissolves, adding the dry carrageenan to the dispersion of microcrystalline **cellulose**, mixing the components, preferably homogenizing the mixture to assure intimate mixing, and drying the mixture. Spray-drying is normally used to. . . .
SUMM [0030] It is possible to prepare the coatings directly, that is, before the drying of the wetcake, from a dispersion of microcrystalline **cellulose** wetcake and the carrageenan, or components of, . . . present in the wetcake and adding the other ingredients in the. . . . coats for a dispersion would be less economical. Fortunately, spray by any method may enhance the association of the microcrystalline **cellulose** with the carrageenan, which may result in a more satisfactory prompt **release** coating.
SUMM [0027] By blended microcrystalline **cellulose** (e.g., Avicel® PH-105, average particle size 20 microns) and iota **carrageenan**, has been found to provide **coating** compositions that are at least equal to, and in some cases, superior to, coating compositions prepared from preprocessed microcrystalline **cellulose**/carrageenan.
SUMM . . . thereof is spread on a surface and allowed to dry. However, the
. . . film is considered to be too weak for **pharmaceutical** tablets as shown by the results in Comparative Example X and therefore requires the

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presence of microcrystalline **cellulose** for satisfactory results.
SUMM [0029] A dry, physical blend of iota carrageenan and microcrystalline **cellulose** (Avicel® PH-105, particle size 100 microns or less) also yielded what appear to be commercially unsatisfactory results in Comparative Example B. Thus, it was unexpected and not to be believed that the average particle size of the microcrystalline **cellulose** used in a dry blend with the iota carrageenan hydrocolloid should be below 100 microns, advantageously below about 50. . . . high performance coating formulations for the purpose of this invention may be prepared from such dry, physical blends of microcrystalline **cellulose** and carrageenan.
SUMM [0030] The weight ratio of microcrystalline **cellulose** to carrageenan in the compositions of this invention may vary depending upon the application, but generally range from about 90:10. . . . different ratios of coprocessed materials or in the dry, physical blends provide significantly greater flexibility for specific applications having different requirements. **Pharmaceutical** and veterinary drug coating forms containing certain active ingredients may require increased carrageenan content in the composition to ideally coat the tablets. For these **pharmaceutical** and veterinary applications, a preferred weight ratio of microcrystalline **cellulose** to carrageenan in the range of about 75:25 to about 65:35.
SUMM [0031] Regardless of whether the composition is based on coprocessed microcrystalline **cellulose**/carrageenan or a dry, physical blend of microcrystalline **cellulose** and carrageenan, a strengthening polymer, preferably, **hydroxyethylcellulose**, a plasticizer or both a strengthening polymer and a plasticizer are preferred in the coating formulation of this invention. While.
SUMM [0032] Other strengthening polymers which can provide the same benefit and may be used instead of HEC include HPMC, **hydroxypropylcellulose**, **ethylcellulose**, **methylcellulose** and **hydroxypropylmethylcellulose** (HPMC); however, care must be exercised in the use of such alternative materials
to avoid significantly retarding **release** of active ingredients and/or bioavailability. The preferred amount of strengthening polymer is less than the total amount of microcrystalline **cellulose** and carrageenan present in the composition. Depending on the desired hardness of the coating, the strengthening polymers may be employed in amounts as is included in the formulation. Strengthening polymers suitable for use in this invention and which will form strong films are known and can be obtained from tablets or other solid dosage forms, are those polymers having a viscosity equal to or less than 20 millideca. . . .
SUMM . . . following optional ingredients are also contemplated and within the scope of the coating compositions of the present invention. The prompt **release** coating compositions of this invention may include at least one filler. Such fillers may include, for example, calcium carbonate, dicalcium . . . carbohydrates, such as starch, maltodextrin, lactose, mannitol and other sugars. Of these, maltodextrin
and mannitol are preferred fillers. The prompt **release** coating compositions of the invention may include at least one surfactant. Such surfactants include either anionic or nonionic surfactants. Useful. . . .
SUMM . . . basis a preferred composition of this invention comprises at least about 45%, suitably about 65% to about 75% of microcrystalline **cellulose** and carrageenan powder combined, more preferably about 65% to about 68%, about 0.5% to about 30% of strengthening polymer, more.

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. . . may be preferable to maintain agitation of the aqueous dispersion during the entire period of its being sprayed onto the **pharmaceutical** or veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizer, pesticide tablets, or the. . . .
SUMM [0039] The preferred edible, hardenable, prompt **release** coating formulations of this invention may generally be prepared and used according to a single procedure. A dry mixture of coprocessed microcrystalline **cellulose** and carrageenan, or a dry blend of microcrystalline **cellulose** and carrageenan, and a strengthening polymer, such as **hydroxyethylcellulose**, a plasticizer glycol or other acceptable plasticizer, optionally together with a solid filler such as maltodextrin, lactose, mannitol, or the like. . . .
SUMM [0040] In the formulations of microcrystalline **cellulose** and iota carrageenan, a single aqueous system provides adequate viscosity for rapid hydration. The period of hydration may be as. . . thixotropic behavior of a formulation which sets up during overnight storage.
Unlike
coating formulations based primarily on hydroxyalkyl ethers of **cellulose**, for example, HPMC, constant stirring of the microcrystalline and carrageenan-based formulations of this invention does not need to be continued.
SUMM . . . Engineering. Equipment variables which one skilled in the art can manipulate to provide an elegant coating based on the microcrystalline **cellulose** and carrageenan materials, either coprocessed or dry blended, include inlet temperature, outlet temperature, air flow, speed of rotation of the. . . .
SUMM [0042] **Hydroxyethylcellulose** binds water more effectively than carrageenan does. Thus, the presence of the major amount of carrageenan in the formulations of. . . the carrageenan which dilutes the negative effect of HEC on drying time. Thus, in the case of low melting active **pharmaceutical** agents, for example, ibuprofen, the outlet temperature can be reduced and still provide short enough drying time to
be commercially. . . .
SUMM [0043] **Hydroxyethylcellulose** is particularly susceptible to clogging spray nozzles at high temperatures. An additional benefit provided by the formulations of this invention is. . . .
SUMM [0044] The level of coating applied to **pharmaceutical** or veterinary dosage forms is preferably sufficient to add 1% to 5% by weight of the uncoated dosage form, more. . . .
SUMM . . . to those of the uncoated tablets used as a substrate for coating. This is an additional unexpected benefit of the **coatings** based on **carrageenan** and microcrystalline **cellulose** that it differs from the known drawbacks of HPMC.
SUMM [0049] All components of the formulation are typically **pharmaceutically** acceptable, edible food grade materials.
DETD [0051] In a Patterson-Kelley twin shell blender were placed 14.43 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), **18.** 36 grams of **hydroxypyrralidone** 29/32 (GAF), 16.40 grams of polyethylene glycol 8000 (Union Carbide Corporation), and 0.2 grams of yellow #5 food color. After. . . .
DETD [0052] By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250-L, Hercules Incorporated), 10.60 grams of polyethylene glycol 8000, and 0.30 gram of yellow #5 food color was added. . . .
DETD [0053] By the method of Example 1, a dry mixture of 19.05 grams of

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spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250L, Hercules Incorporated), 0.60 gram of polyethylene glycol 8000, 5.0 grams of Micro-Talc, and 0.30 gram of red.

DETD (0054) By the method of Example 1, a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250L, Hercules Incorporated), 10.40 grams of polyethylene glycol 8000, and 0.70 gram of yellow #5 food color was added.

DETD (0055) By the method of Example 1, a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250L, Hercules Incorporated), 10.40 grams of polyethylene glycol 8000, 0.10 gram of yellow #5 food color, and 0.10 gram of red #3 coloring. The resulting solution was sprayed using a Vector High Coater LDCS onto 1 Kg of cores comprised of 20% microcrystalline **cellulose** and 80% calcium carbonate, each weighing on average 1.05 grams. Conditions used include an inlet temperature of 73-80° F.

DETD (0056) By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 10.65 grams of polyethylene glycol 8000, and 0.70 gram of yellow #5 food color was added to 600 grams of deionized. . . . stirred while it was sprayed using a Vector High Coater LDCS onto 1 Kg of the same cores of microcrystalline **cellulose** and calcium carbonate that were coated in Example 4. Conditions used include an inlet temperature of 78-79° C., an outlet. . . in purified water at 37° . . . wa less than 3 minutes. This coating layer was applied as coatings containing **hydroxyethylcellulose**.

DETD (0057) By the method of Example 1, a dry mixture of 20.95 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota carrageenan (70:30), 6.55 gram of hydroxypropyl methylcellulose, 11.40 grams of polyethylene glycol 8000, and 0.20 gram of yellow iron oxide was added to 450 grams of. . . suction was continuously applied while it was sprayed using a Vector Bush Coater LDCS onto 1.00 Kg of compressed microcrystalline **cellulose** and lactose® 80 mesh blended with an FMC logo, each weighing on average 0.267 gram. Conditions used include an inlet temperature.

DETD (0058) By the method of Example 1 a dry mixture of 285.75 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (90:10), 7.5 grams of **hydroxyethylcellulose** 250L, 156.0 grams of polyethylene glycol 8000, 45.0 grams of Hydrophilic red iron oxide was prepared. A portion (60. . . . have as elegant an appearance as those prepared in Examples 1 through 7 in which the 70:30 combination of microcrystalline **cellulose** and iota carrageenan was employed. Friability testing was satisfactory, but there was minor chipping and erosion observed for these coated.

DETD (0059) By the method of Example 1 a dry mixture of 390.8 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota carrageenan (70:30), 5.02 grams of **hydroxyethylcellulose** 250L, 104.2 grams of polyethylene glycol 8000, 1.68 grams of methyl paraben, 0.15 gram of propyl paraben, 18.48 grams of. . . .

DETD (0062) By the method of Example 1 a dry mixture of 194.7 grams of

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dye blend (Warner Jenkinson). . . .

DETD (0068) In a large Patterson-Kelley twin shell blender were placed 1.940 Kg of a blend of microcrystalline **cellulose** (Avicel® PH-105, 1.358 Kg) and iota carrageenan (0.582 Kg), 0.436 Kg of **hydroxyethylcellulose** (Aqualon® 250L), 0.277 Kg of sucrose (Maltrin® M-180, Grain Processing Corporation), and 1.307 Kg of polyethylene glycol 8000 (Union Carbide. . .

DETD (0070) In a Patterson-Kelley twin shell blender were placed 72.80 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 56 .**25** grams) and iota **carrageenan** (16.2 grams), 33.00 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 44.15 grams of hydrophilic red iron oxide. After being thoroughly mixed, the dry components were added to. . .

DETD (0071) In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (18.5 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), 15.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), and 22.0 grams of hydrophilic yellow oxide. After being. . .

DETD (0072) In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (18.5 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 21.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation). Simultaneously 22.5 grams of titanium dioxide was added.

DETD (0073) In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (18.5 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 12.0 grams of maltodextrin (Maltrin M-100, Grain Processing Corporation). Simultaneously 31.5 grams of titanium dioxide was added.

DETD (0074) In a Patterson-Kelley twin shell blender were placed 78.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**22**.5 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 9.0 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation). Simultaneously 30.0 grams of titanium dioxide was added. . . .

DETD (0075) In a Patterson-Kelley twin shell blender were placed 71.33 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 49.94 grams) and iota **carrageenan** (**21** .39 grams), 16.01 grams of **hydroxyethylcellulose** (Aqualon® 250L), 68.05 grams of polyethylene glycol 8000 (Union Carbide Corporation), 10.19 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation). . . .

DETD (0076) In a Patterson-Kelley twin shell blender were placed 78.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**22**.5 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 1.5 gram of stearic acid. Simultaneously 37.5 grams of titanium dioxide was added to 1516.7 grams of. . . .

DETD (0077) In a Patterson-Kelley twin shell blender were placed 300 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, **200** grams) and iota **carrageenan** (**100** grams), and **100** grams of polyethylene glycol 8000 (Union Carbide Corporation). After the dry components had been thoroughly blended, the entire blend was. . . .

DETD (0078) In a Patterson-Kelley twin shell blender were placed 49.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 36.3

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spray-dried, coprocessed microcrystalline **cellulose**/iota carrageenan (70:30), 5.61 grams of **hydroxyethylcellulose** 250L, 104.4 grams of polyethylene glycol 8000, 1.65 grams of methyl paraben, 0.165 gram of propyl paraben, 18.48 grams of. . . .

DETD (0061) By the method of Example 1, a dry mixture of 68.94 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 1.82 grams of **hydroxyethylcellulose** 250L, 37.63 grams of polyethylene glycol 8000, 0.545 grams of methyl paraben, 0.0545 gram of propyl paraben, 10.24 grams of.

DETD (0062) In a Patterson-Kelley twin shell blender were placed 229.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 160.65 grams) and iota carrageenan (68.85 grams), 49.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 148.5 grams of polyethylene glycol 8000 (Union Carbide Corporation), 13.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation). . . .

DETD (0067) By the method of Example 1, a dry mixture comprising 238.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 166.95 grams) and iota carrageenan (71.55 grams), 61.8 grams of **hydroxyethylcellulose** (Aqualon® 250L), 148.5 grams of polyethylene glycol 8000 (Union Carbide Corporation), and 22.5 grams of maltodextrin (Maltrin M-180), was dispersed. . . 90° C. Dyestuction required 75 minutes. A Accela-Cota coater was charged with 12 Kg of cores comprised of 20% microcrystalline **cellulose** and 80% calcium carbonate, each weighing on average 1.05 grams. The coater was operated at an inlet temperature of 92.8-108.3°.

DETD (0065) In a Patterson-Kelley twin shell blender were placed 234.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 166.5 grams) and iota carrageenan (67.5 grams), 67.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 63.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), 10.8 grams of titanium dioxide, and 22.5 grams of.

DETD (0066) In a Patterson-Kelley twin shell blender were placed 76.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**21**.0 grams), **22**.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 28.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), 10.9 grams of Fed #40 aluminum lake, and 0.7.

DETD (0067) In a Patterson-Kelley twin shell blender were placed 76.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota carrageenan (18.5 grams), and 0 grams of **hydroxyethylcellulose** (Aqualon® 250L), 28.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), 10.9 grams of a red

L57 ANSWER 23 OF 79 USPATFULL on STN (Continued)
grams) and iota **carrageenan** (**14**.7 grams), **11**.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), 33.0 grams of polyethylene glycol 8000 (Union Carbide Corporation), 7.0 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation). . . .

DETD (0080) In a Patterson-Kelley twin shell blender were placed 43.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 33 grams) and iota **carrageenan** (**10** grams), **20** grams of **hydroxyethylcellulose** (Aqualon® 250L), 23.0 trams of triacetin, 6.8 grams of propylene glycol alginate, and 3 grams of Pluronic F-68 (BASF). After. . . .

DETD . . . was prepared by dry blending to provide a coating composition having the following formulation:

Ingredient	Amount (g)
Microcrystalline **cellulose** (Avicel PH-**105**)	37.5
Iota **carrageenan**	**14**.7
Polyethylene glycol 8000	34
Hydroxyethylcellulose 250 L	11
Maltodextrin M-180	3

DETD . . . formulations shown in the following table:

Example:	Weight (grams) 31	32	33
Avicel PH-105	39	34.3	34.3
Iota **carrageenan**	15	**14**.7	**14**.7
Hydroxyethylcellulose	--	11	11
PGA sup.a	7		
PEG sup.b	34	33	33
Lecithin sup.c	3	4	7
Maltrin M-180	3	3	

sup.aPropylene glycol alginate (Protonal. . . .

DETD . . . example were dry blended to provide the dry coating composition shown in the following tables:

	Weight (grams)
Avicel PH-105	33
Iota **carrageenan**	**10**
Hydroxyethylcellulose	**20**
PGA sup.a	4
Pluronic F-68	3

sup.aPropylene glycol alginate (Protonal ® ester SD-LB, Pronova).

DETD . . . , tablets which were tested for friability. This example is summarized in the following table:.

Ingredient	Weight (grams)

L57 ANSWER 23 OF 79 USPATFULL on STN (Continued)

Avicel PH-105	37	
Iota **carrageenan**	145	
Hydroxyethylcellulose	22	
Mannitol,sup.a	15.5	
Pluronic F-68	9	
Blue Lake #2	0	
Deionized water	1150	
Hydration time	2.5	
Caplets		
Ibuprofen	1	kg

Acetaminophen . . .

DETD [0099] A dispersion of 9.30 grams of microcrystalline **cellulose** (Avicel® PH-121, FMC Corporation) and 20.7 grams of iota carrageenan (Viscarin® SD-389) in 1500 grams of deionized water was prepared. . .

CLM What is claimed is:

1. An edible, hardenable, prompt-**release** coating composition comprising (a) microcrystalline **cellulose**, (b) a film forming amount of carrageenan, and (c) at least one of a strengthening polymer and a plasticizer, wherein said coating composition does not, when ingested or

placed in an aqueous medium, significantly retard **release** of active ingredients from a substrate to which said coating is applied.

CLM What is claimed is:

2. The coating composition of claim **1**, wherein the **carrageenan** is iota carrageenan.

CLM What is claimed is:

4. The coating composition of claim 3, wherein said strengthening polymer is selected from the group consisting of **hydroxyethylcellulose**, **hydroxypropylmethylcellulose**, **hydroxypropylcellulose**, **ethylcellulose**, **methylcellulose**, and **polyvinylpyrrolidone**.

CLM What is claimed is:

5. The coating composition of claim 3, wherein the strengthening polymer

is **hydroxyethylcellulose**.

CLM What is claimed is:

15. The coating composition of claim 1, wherein the weight ratio of microcrystalline **cellulose** to carrageenan is in the range of about 90:10 to about 60:40.

CLM What is claimed is:

17. The coating composition of claim 1, wherein the microcrystalline **cellulose** has an average particle size in the range of 1 to 50 microns.

CLM What is claimed is:

18. The coating composition of claim 17, wherein the microcrystalline **cellulose** has an average particle size in the range of about 1 to

L57 ANSWER 23 OF 79 USPATFULL on STN (Continued)

about 30 microns.

CLM What is claimed is:

20. A dry coating composition comprising a dry blend of microcrystalline **cellulose**, carrageenan and at least one of a strengthening polymer and a plasticizer.

CLM What is claimed is:

21. The coating composition of claim 1 or 20, comprising at least 40% by

weight of microcrystalline **cellulose** and carrageenan, from about 0.5% to about 30% strengthening polymer, optionally comprising, about 25% to about 40% plasticizer.

CLM What is claimed is:

22. A coating composition of claim 21, comprising by weight about 40% to

about 60% microcrystalline **cellulose** and carrageenan, about 7% to about 22% strengthening polymer, and about 3.4% to about 25% plasticizer.

CLM What is claimed is:

27. The coating composition of claim 22, wherein the strengthening polymer is **hydroxyethylcellulose** and the plasticizer is selected from the group consisting of polyethylene glycol and triacetin.

CLM What is claimed is:

24. An aqueous dispersion comprising a coating composition of the edible, hardenable, prompt-**release** coating composition of claim 1.

CLM What is claimed is:

27. An aqueous dispersion of a composition of claim 1, 2, or 3, wherein said microcrystalline **cellulose** and carrageenan are present in a weight ratio of about 70:70; said strengthening polymer is selected from

the group consisting of **hydroxyethylcellulose**, **hydroxypropylmethylcellulose**, **methylcellulose**, **ethylcellulose**, **hydroxypropylcellulose** and **polyvinylpyrrolidone**; said plasticizer is selected from at least one of the group consisting of polyethylene glycol, triacetin, dibutyl sebacate, propylene glycol, . . .

CLM What is claimed is:

28. An aqueous dispersion of a composition of claim 19, wherein said microcrystalline **cellulose** and carrageenan are present in a weight ratio of about 70:30.

CLM What is claimed is:

29. A **pharmaceutical** or veterinary solid dosage form coated with an edible, hardenable, prompt-**release** coating composition of claim 1.

CLM What is claimed is:

30. The **pharmaceutical** or veterinary solid dosage form of claim 29, wherein the coating is applied to the solid dosage form at a. . .

CLM What is claimed is:

L57 ANSWER 23 OF 79 USPATFULL on STN (Continued)

31. The **pharmaceutical** or veterinary solid dosage form of claim 30, wherein the coating is applied to the dosage form at a level. . .

CLM What is claimed is:

32. A **pharmaceutical** or veterinary tablet coated with the aqueous dispersion of claim 28.

CLM What is claimed is:

34. A coating composition for use in lieu of a sugar **coating** consisting of microcrystalline **cellulose**, **carrageenan**, and polyethylene glycol.

CLM What is claimed is:

35. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, high molecular weight polyethylene glycol and maltodextrin, wherein said microcrystalline **cellulose** has a particle size less than 50 microns.

CLM What is claimed is:

36. A **pharmaceutical** solid dosage form comprising the edible coating composition of claim 35.

CLM What is claimed is:

38. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, mannitol, a surfactant and a coloring agent, wherein said microcrystalline **cellulose** has a particle size less than 50 microns.

CLM What is claimed is:

39. A **pharmaceutical** solid dosage form comprising the edible coating composition of claim 38.

CLM What is claimed is:

41. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, and a coloring agent, wherein said microcrystalline **cellulose** has a particle size less than 50 microns.

CLM What is claimed is:

42. A **pharmaceutical** solid dosage form comprising the edible coating composition of claim 41.

CLM What is claimed is:

44. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, high molecular weight polyethylene glycol and a coloring agent, wherein said microcrystalline **cellulose** has a particle size less than 50 microns.

CLM What is claimed is:

46. A dry **coating** composition comprising microcrystalline **cellulose**, **carrageenan** and at least one of a strengthening polymer and a plasticizer, wherein said dry composition can be hydrated in a. . .

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ACCESSION NUMBER:	2002:146674 USPATFULL
TITLE:	Edible MCC/PGA coating composition
INVENTOR(S):	Kupilla, Michael, Marlboro, NY, United States Dell, Sheila M., New Hope, PA, United States Kliefirnich, Eric K., Yardville, NJ, United States
PATENT ASSIGNEE(S):	FMC Corporation, Philadelphia, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6504462	B1	20021231	
APPLICATION INFO.:	US 2000-696780		20001026 (9)	<--

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-217499P	20000711 (60)	<--
	US 2000-189888P	20000315 (60)	<--
	US 1999-172526P	19991217 (60)	<--
	US 1999-167487P	19991124 (60)	<--
	US 1999-162514P	19991029 (60)	<--

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Page, Thurman K.
ASSISTANT EXAMINER:	Tran, S.
LEGAL REPRESENTATIVE:	Woodcock Washburn LLP
NUMBER OF CLAIMS:	20
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT:	728

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable coating composition is disclosed containing microcrystalline **cellulose**, a film forming amount of propylene glycol alginate, and a strengthening polymer, optionally in combination with at

least one of a plasticizer, a surfactant, or a filler. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt

release coating which does not retard the **release** of active ingredients from the coated substrate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable coating composition is disclosed containing microcrystalline **cellulose**, a film forming amount of propylene glycol alginate, and a strengthening polymer, optionally in combination with at

least one of a plasticizer, a surfactant, or a filler. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt

release coating which does not retard the **release** of active ingredients from the coated substrate.

SUMM This invention relates to edible, hardenable coating compositions comprising microcrystalline **cellulose** (MCC), a film forming amount of

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propylene glycol alginate (PGA) and a strengthening polymer, optionally containing a plasticizer, a surface. . . a coloring agent or a combination of such optional ingredients. The coatings of the present invention can be applied to **pharmaceutical**, including nutraceutical, and veterinary solid dosage forms, such solid substrates such as seeds, animal feed, fertilizers, pesticide tablets and granules. . . dispersed in aqueous media, and, when applied as a coating, provide high
luste coatings, which do not retard or extend **release** of active
SUM=1 ingredient from a coated substrate.
SUM=1 It is a common practice to coat **pharmaceutical** and veterinary tablets to obtain several advantages among being there are to improve the surface characteristics of tablets to make them
SUM=1 Another very important function of the **pharmaceutical** or veterinary tablet coating is to improve the integrity of the tablet itself. Uncoated tablets are often subject to . . .
SUM=1 A particular disadvantage of coatings based primarily on **hydroxypropylmethylcellulose** is that the tend to dry out, harden over time and therefore increase tensile tablet disintegration times. An increase in disintegration time . . . ingredients to the increase in disintegration time. Many other agents commonly used in coating compositions are also known to delay **release** of **pharmaceutical** agents, such as enteric coatings which use polymeric film forming materials which are insoluble in water, or gastric fluid, some of these being specifically selected to by-pass both the stomach and small intestine and provide colonic **release**.
SUM=1 The coatings of this invention meet U.S. **Pharmacopeia** standards for rapid or immediate dissolution (U.S.P. monograph 23) of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or dissolution of the active with the **release** rates which is normally obtained with the uncoated tablets or other substrates. Thus, they do not adversely impact the rate of **release** of active ingredients from a substrate coated with them. Further, the coatings of this invention are readily dispersed and rapidly. . .
SUM=1 . . . accordance with the present invention by a coating composition which comprises a unique combination of materials specifically adapted for prompt **release** when placed in aqueous media or ingested. The coating composition of the present invention comprises microcrystalline **cellulose**, a film forming amount of propylene glycol alginate and a strengthening polymer, and may contain a plasticizer, a . . . a surface. . . agent, a filler, a coloring agent or combination of these additional ingredients. More specifically, the present invention provides a prompt **release**, edible, hardenable coating composition, as well as dry coatings and aqueous dispersions thereof and solid dosage forms coated therewith.
SUM=1 . . . application, the term "edible" is intended to mean food grade materials which are approved by regulatory authorities for use in **pharmaceutical** or food applications. The term "hardenable," used to describe the coating compositions of this invention, is intended to include only . . . this composition is combined with the . . . compositions of this invention, mean that the coatings of this
invention
meet U.S. **Pharmacopeia** standards (U.S.P. monograph 23) for rapid or immediate dissolution of active ingredients from tablets or other solid

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blended in any suitable manner, such as dry blending. Dry blended microcrystalline **cellulose**, for example, Avicel® PH-105, average particle size 20 microns and propylene glycol alginate have been found to provide coating compositions . . .
SUM=1 . . . to be too weak to provide a satisfactory coating. But, when a film forming amount thereof is blended with microcrystalline **cellulose** having, for example, a particle size below 100 microns, preferably in the range of about 1-50 microns, more preferably, about . . .
SUM=1 Propylene glycol alginate may be used in combination with other film forming materials, for example, carrageenan and **cellulosic** polymers such as HPMC and **hydroxypropylcellulose**.
SUM=1 . . . glycol alginate at a concentration in the range of about 3% to about 20% of the dry weight of the coating composition. . . . **carrageenan** is employed in the composition at a concentration in the range of about 5% to about 15% by weight thereof. . . .
SUM=1 The weight ratio of microcrystalline **cellulose** to propylene glycol alginate in the composition of this invention may vary depending on
the
application, but generally range from.
SUM=1 A dry, physical blend of microcrystalline **cellulose** and a film forming amount of propylene glycol alginate, a strengthening polymer, preferably, **hydroxyethylcellulose** (HEC), are present in the coating formulation of this invention, advantageously in combination with other optional ingredients such as a. . . combinations thereof. Other strengthening polymers which can provide the same benefit may be used instead of HEC include HPMC, **hydroxypropylcellulose**, **ethylcellulose**, **methylcellulose** and **polyvinylpyrrolidone** (PVP), however care must be exercised in the use of such alternative materials to avoid retarding **release** of active ingredients and/or
bioavailability.
SUM=1 The preferred amount of strengthening polymer is less than the total amount of microcrystalline **cellulose** and propylene glycol alginate present in the composition. Depending on the desired hardness of the coating, the strengthening polymer may . . . another strengthening polymer is analogous to the formulation. Strengthening polymers suitable for use in this invention, which will not retard **release** from tablets or other solid dosage forms, are those polymers having a viscosity
equal
SUM=1 to or less than 20 mPa.s.
SUM=1 On a dry weight percentage basis the composition of this invention comprises from about 15% to about 50% of microcrystalline **cellulose**, about 30% to about 50% by weight of propylene glycol alginate, and
about
SUM=1 5% to about 25% of strengthening polymer.
SUM=1 . . . may be preferable to maintain agitation of the aqueous dispersion during the application of the coating to the . . . being used in the **pharmaceutical** or veterinary solid dosage forms, confectionery, snacks, animal feed, fertilizer, pesticide tablets, or food.
SUM=1 The preferred edible, hardenable, prompt **release** coating formulations of this invention may generally be prepared and used according to a simple procedure. A dry blend of microcrystalline **cellulose** and propylene glycol alginate, and a strengthening polymer, such as **hydroxyethylcellulose**, and optionally at least one additional ingredient, such as polyethylene glycol or other acceptable
plasticizer,
optionally together with a solid. . .
SUM=1 In the formulations of microcrystalline **cellulose** and propylene glycol alginate, a simple propeller mixer provides adequate agitation for
rapid

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dosage forms coated with them. Thus, they provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrate. They do not,
when
placed in water or ingested, adversely impart or retard **release** or dissolution of tablets or other dosage forms coated with them. Coatings made in accordance with the present invention are . . .
SUM=1 The microcrystalline **cellulose**, amply blended with propylene glycol
as
SUM=1 elegant coating which is particularly useful in, for example, coating **pharmaceutical** and veterinary tablets, caplets, granules, and spheres which contain active ingredients which require **release** promptly after being placed in aqueous media, or ingested.
SUM=1 Microcrystalline **cellulose** is a purified, partially depolymerized **cellulose** that is generally produced by treating a source of **cellulose**, preferably alpha **cellulose** in the form of pulp from fibrous plants, with a mineral acid, preferably hydrochloric acid. The acid selectively attacks the less ordered regions of the **cellulose** polymer chain, thereby exposing and freeing the crystalline sites, forming the crystalline aggregates which constitute microcrystalline **cellulose**. These are then separated from the reaction mixture and washed to remove degraded by-products. The resulting wet mass,
generally
containing 40 to 60 percent moisture, is referred to in the art by several names, including hydrolyzed **cellulose**, microcrystalline **cellulose**, microcrystalline **cellulose** wetcake, or simply wetcake. This microcrystalline **cellulose** wetcake may be used as such or may be further modified, for example, by attrition and/or drying, and utilized in.
SUM=1 Microcrystalline **cellulose** may also be produced for use in the present invention using a steam explosion treatment. In this process, wood
chips
or other **cellulosic** materials are placed in a chamber into which super-heated steam is introduced. After being maintained for a period
of
about 1-5 minutes, the exit valve is opened rapidly, **releasing** the contents explosively and yielding microcrystalline **cellulose**. No additional acid need be introduced into the reaction mixture, since it is believed that the acidic conditions of the wood at the . . . elevated
temperature and pressure hydrolyze the **celluloses** and degrade it. In addition to the specific forms of microcrystalline **cellulose**, the present invention also contemplates the use of other **cellulose** derivatives, including microcrystalline **cellulose**, also known as microcrystalline microcrystalline **cellulose**, and powdered **cellulose** such as a commercial material sold as "Solka Floc®."
SUM=1 As discussed in greater detail below, the microcrystalline **cellulose** preferred for use in the present invention is microcrystalline **cellulose** which has an average particle size below about 100 microns, preferably microcrystalline **cellulose** which has been attrited so has an average particle size in the range of 1 to 50 microns, preferably 1.
SUM=1 The microcrystalline **cellulose** and propylene glycol alginate may be

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hydration. The period of hydration may be. . . . thixotropic behavior of a formulation which sets up during overnight storage. Unlike coating formulations based partially on hydroxypalkyl ethers of **cellulose**, for example, HPMC, constant stirring of the microcrystalline and propylene glycol alginate-based formulations of this invention does not need to.
. . .
SUM=1 . . . variables which one skilled in the art can manipulate to provide an elegant coating based on dry blends of microcrystalline **cellulose** and propylene glycol alginate, include inlet temperature, outlet temperature, air flow, speed of rotation of the coating pan, and the.
SUM=1 **Hydroxypropylcellulose** binds water more effectively than propylene glycol alginate does. Thus, the presence of the major amount propylene glycol alginate in. . . glycol alginate which dilutes the negative effect of HPC on drying time. Thus, in the case of coating active **pharmaceutical** agents, for example, ibuprofen, the outlet temperature can be reduced and still provide short enough drying times to be commercially.
SUM=1 **Hydroxypropylcellulose** is particularly susceptible to clogging spray nozzles at high temperatures. An additional benefit provided by the formulations of this invention.
SUM=1 The level of coating applied to **pharmaceutical** or veterinary dosage forms is preferably between about 0.5% to about 4% by weight of the uncoated dosage form, more.
SUM=1 . . . a substrate for coating. This is an additional unexpected benefit of the coatings based on propylene glycol alginate and microcrystalline **cellulose**, and it differs from the known drawbacks of coating formulations in which HPMC is the primary or only film-former.
SUM=1 All components of the formulation are typically **pharmaceutically** acceptable, edible food grade materials.
DETD In a Patterson-Kelly twin shell blender were placed 48.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 35 grams) and propylene glycol alginate (13 grams), 20 grams of **hydroxypropylcellulose** (Aqualon®250L), 25 grams of triacetin, and 3 grams of Pluronic F-68 (BASF). After the dry components had been thoroughly blended. . .

DETD
TABLE 1

Examples: 2 3 4 5

Ingredient Weight (grams)
Avicel PH-105 37 35 37 37
Hydroxypropylcellulose 22 20 22 22
PGA.sup.a 12 13 12 12
Pluronic F-68 3.5 3 -- 1.5
hcd #40 dispersion 24.5 4.6 7.5
Triacetin -- 25 -- --
Mannitol.sup.b -- -- **18 15**
Iota **carrageenan** -- -- 5 5
Deionized water 1013.1 1013.1 1013.1 1013.1
Hydration time 2 hours >1 hour 6 hours >1 hour
Caplets Charge (Kg) . . .
Acetaminophen. . . .
DETD
TABLE 2

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Example: 6

Ingredients Weight (grams)
Avicel PH-101 37
PGA sup.a 13
Soda **carrageenan** 5
Hydroxyethylcellulose 22
Mannitol.sup.b 27.5
Fluronic F-68 3.5
Blue Lake #2 2
Deionized water 135G
Hydration time 2 hours
Caplets Charge 8vg
Ingredients. . . .
DETD 35
HEC 30 10 5 - - - 15 15
Lecithin.sup.b 0 3 3 3 - - 3 2 2 17
Maltodextrin M10@ 17 17 17 25 **22 17 17**
Soda **Carrageenan** 5 5 5 5 5 5 5 5
Red hydrophilic 5 5 5 5 - - 15 10 - -
Iron Oxide
Blue lake/ - - - - -
DETD 39 20 20 15 20
Hydroxyethyl- 15 15 17 20 22 20 20 20 20 20 17 15 20 15 **20 20**
cellulose
Soda **carrageenan** 5 5 5 5 12 12 12 12 15 15 15 12 12 12 12 10
Lecithin.sup.b 3 3 5 -

CLM What is claimed is:
1. An edible, hardenable, prompt **release**, **pharmaceutical** and veterinary solid dosage form coating composition comprising (a) microcrystalline **cellulose** having an average particle size less than 100 microns, (b) a film forming amount of propylene glycol alginate, (c) a . . . (d) at least one of a plasticizer, a surface active agent and a filler, wherein the weight ratio of microcrystalline **cellulose** to propylene glycol alginate is in the range of 90:10 to 20:80 wherein said

prompt **release**, **pharmaceutical** and veterinary solid dosage form coating composition does not, when ingested or placed in aqueous media, adversely retard **release** or dissolution of active ingredients from a **pharmaceutical** or veterinary solid dosage form to which said coating composition is applied.

CLM What is claimed is:
2. The coating composition of claim 1, comprising 5% to 50% by weight microcrystalline **cellulose**, 10% to 50% by weight propylene glycol alginate, and 5% to 25% by weight strengthening polymer.

CLM What is claimed is:
4. The coating composition of claim 1 in which the strengthening polymer

is **hydroxyethylcelluloses**.

CLM What is claimed is:
10. The coating composition of claim 1, wherein the microcrystalline

L57 ANSWER 24 OF 79 USPATFULL on STN (Continued)
cellulose has an average particle size in the range of 1 to 50 microns.

CLM What is claimed is:
11. The coating composition of claim **1**, further comprising **carrageenan** in an amount of from 3% to 20% by dry weight of the composition.

CLM What is claimed is:
12. The **coating** composition of claim **11**, wherein **carrageenan** is present in an amount in the range of 3% to 8% by dry weight of the composition and the. . .
CLM What is claimed is:
15. The composition of claim **11** wherein **carrageenan** is present in an amount in the range of 9% to 20% by dry weight of the composition and the. . .
CLM What is claimed is:
18. A method for forming an edible, hardenable, prompt **release**, **pharmaceutical** and veterinary solid dosage form coating composition comprising: i) combining (a) microcrystalline **cellulose** having an average particle size less than 100 microns, (b) a film forming amount of propylene glycol alginate, (c) a. . . the ramds of 9010 20:80; and

ii) forming a film coating by spraying an aqueous suspension of i) onto a **pharmaceutical** or veterinary solid dosage form, wherein said prompt **release**, **pharmaceutical** and veterinary solid dosage form coating composition does not, when ingested or placed in aqueous media, adversely retard **release** or dissolution of active ingredients from said **pharmaceutical** or veterinary solid dosage form to which said coating composition is applied.
CLM What is claimed is:
19. A method of coating **pharmaceutical** and veterinary solid dosage forms comprising the steps of hydrating the coating composition of claim

1, followed by spray coating said hydrated coating composition onto a **pharmaceutical** or veterinary solid dosage form.

CLM What is claimed is:
20. An edible, hardenable, prompt **release**, **pharmaceutical** and veterinary solid dosage form coating composition comprising (a) microcrystalline **cellulose**, (b) a film forming amount of propylene glycol alginate, (c) a strengthening polymer and optionally (d) at least

one of a plasticizer, a surface active agent and a filler, wherein the weight ratio of microcrystalline **cellulose** to propylene glycol alginate is in the range of 90:10 to 20:80 and wherein said prompt **release**, **pharmaceutical** and veterinary solid dosage form coating composition does not, when ingested or placed in aqueous media, adversely retard **release** or dissolution of active ingredients from a **pharmaceutical** or veterinary solid dosage form to which said coating composition is applied.

L57 ANSWER 25 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2002:137910 USPATFULL
TITLE: LOW-DENSITY COMPOSITIONS AND PARTICULATES INCLUDING GUMS
INVENTOR(S): Christensen, Robert I., JR., Pinole, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20020137275	A1	20021219
	US 6583099	B2	20030624
APPLICATION INFO.:	US 2002-187781	A1	20020701 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-479693, filed on 7 Jan 2000, ABANDONED		

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-115255P	19990108 (60)	<--
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Novozymes International, Inc., 925 Page Mill Road, Palo Alto, CA, 94304-1013		
NUMBER OF CLAIMS:	23		
EXEMPLARY CLAIM:	1		
LINE COUNT:	879		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB . . . The present invention provides low-density compositions, as well as particulates formed, at least in part, from such compositions.
Preferred

low-density materials include, for example, hollowspheres, low-density minerals, and low-density wood materials (e.g., sawdust). The

low-density compositions of the invention can be formed as particulates,

or cores, suitable for use in forming enzyme granules, e.g., naruna, layered granules, prills, drum granules, agglomerated granules, or the like. Granules are disclosed having advantageous properties, e.g., low dusting, storage stable, fast enzyme-**release** profile, low true density, etc. The granules of the invention are especially useful, for example, in liquid detergents and cleaners, such as predominantly aqueous, liquid laundry detergents. In one embodiment, granules are provided having a true, or volumetric, density within a range of from about 0.95 to about 1.4 g/cm.sup.3. The granules can be economically produced in commercial quantities by way of a narrowcirculation, drum granulation, fluid-bed spray-coating, pan-coating, or other suitable process.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB . . . prills, drum granules, agglomerated granules, or the like. Granules are disclosed having advantageous properties, e.g., low dusting, storage stable, fast enzyme-**release** profile, low true density, etc. The granules of the invention are especially useful, for example, in liquid detergents and cleaners.
SUMM [0003] The use of proteins such as **pharmaceutically** important proteins, e.g., hormones, and industrially important proteins, e.g., enzymes, has been rapidly growing in recent years. Today, for example,. . .
SUMM . . . U.S. Pat. No. 4,106,991 describes an improved formulation of enzyme granules by including within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-20% w/w

L57 ANSWER 25 OF 79 USPATFULL on STN (Continued)
based on the dry weight of the whole composition. In addition, this patent.
SUMM . . . distemaceous earth or sodium citrate crystals. The film forming

material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.
SUMM . . . of providing sufficient enzyme activity in the wash. It is also

generally desirable to have granule with a relatively fast **release** profile. Thus, the enzyme load for each granule needs to be protected from the various harsh components of the. . . detergent, such as perboate

or sodium percarbonate, and the like), yet the means of achieving such protection must not unduly hinder enzyme **release**. As is well known by those working in the field, it is often problematic to simultaneously provide good protection for the enzyme and a fast **release** profile.
SUMM . . . detergent environment so that they remain active throughout the

product lifecycle. It is also desirable to have a relatively fast enzyme-**release** profile.
SUMM . . . a true density less than 1.4 g/cm.sup.3; they exhibit sufficient enzyme activity in the wash; they have a relatively fast enzyme-**release** profile; they have relatively low susceptibility to attritional breakdown; they tend to remain dispersed and suspended in the liquid detergent.
SUMM . . . in storage (e.g., greater than 50%). Moreover, an especially desirable granule would additionally disintegrate quickly in the wash liquor to **release** its enzyme activity. It is an advantage of the present invention to provide granules meeting such specifications.
SUMM . . . dent starch, modified starches (e.g., hydroxypropyl; addition, ethoxylation, acetylation), acid thinning (e.g., reacting with acid, dextroses, fructoses, lactoses etc.), maltodextrin, **polyvinylpyrolidone** (PVP), polyethylene glycol (PEG), xanthum gum, gum arabic, acacia gum, alginate, carageenan, waxes (e.g., carnuba, beeswax, paraffin and blends

thereof),.
SUMM [0051] Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as enzymes.
SUMM [0057] Suitable coatings include water soluble or water dispersible film-forming polymers such as **polyvinyl** alcohol (PVA); polyvinyl pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose** (MC), hydroxypropyl **methylcellulose** (HPMC), hydroxyethyl **cellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, gum arabic, xanthan, **carrageenan**, chitosan, later polymers, and enteric **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.
SUMM . . . Preferably, the water coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVA-methylmethacrylate copolymer and PVP-PVA copolymer and enteric co-polymers such as those sold under the. . .
DETD . . . dessert-60 fluid bed coater and fluidized. To this, 65.8 Kgs of a solution containing 7.3% active alkaline protease and 2.1%

L57 ANSWER 25 OF 79 USPATFULL on STN (Continued)
polyvinylpyrrolidone (Luviskol K-17 from BASF) was spray-coated onto the cores. Subsequently, a 40% solids solution containing 6.8 Kg of dry corn . . . Kgs of hydrolyzed starch was spray-coated onto the enzyme particulates. Finally, a cosmetic coating solution containing 3.62 Kgs of hydroxyethyl **cellulose** (Methocel E from Dow chemical), 4.352 Kgs of titanium dioxide and 0.731 Kgs of polyethylene glycol (PEG 8000) was spray-coated. . .
DETD [0085] c) 600 grams of **cellulose** fibers (Arbocel 600-30)
DETD [0089] g) 39 grams of **polyvinylpyrrolidone** (Luviskol K-30 from BASF)
DETD . . . of 85° C. finishing at. 70 this, 1750 grams of a 17%
w/w total solids solution containing 25 grams of **polyvinyl** pyrolidone and 1665 grams of a liquid enzyme concentrate containing 7.4% alkaline protease was spray-coated onto the low density marume. . . coated onto the enzyme marume. Subsequently, 1,500 grams of a 13% w/w total solids solution including 82 grams of hydroxypropylmethyl **cellulose** (Methocel E-15), 99 grams of titanium dioxide and 17 grams of polyethylene glycol (PEG600) was overcoated onto the marume as. . .
DETD [0090] c) 600 grams of **cellulose** fibers (Arbocel 600-30)
DETD [0100] g) 39 grams of **polyvinylpyrrolidone** (Luviskol K-30 from BASF)
DETD . . . coated onto the enzyme marum. Subsequently, 1520 grams of a 13%
w/w total solids solution including 74 grams of hydroxypropylmethyl **cellulose** (Methocel E-15), 89 grams of titanium dioxide, 20 grams of needel 23/6.5 (Shell chemicals) and 15 grams of polyethylene glycol. . .
DETD . . . was spray-coated onto the sucrose seeds. Subsequently, 56.3 Kgs
of a 13% w/w total solids solution containing 3.3 Kgs hydroxypropylmethyl **cellulose** (Methocel E-15), 3.3 Kgs titanium dioxide and 0.7 Kgs of polyethylene glycol (PEG 600) was spray coated onto the enzyme. .
DETD [0112] Enzyme **Release**
DETD [0113] A commonly used method for measuring enzyme **release** from a granule under typical laundry application conditions is the enzyme dissolution test. In this test, granules are added to. . .
DETD [0114] Granules of the present invention preferably have at least 80%, and preferably at least 90%, of the enzyme activity **released** into the liquor within 5 minutes at 15° C. More preferably, the granules taught herein have a minimum of 90% of the enzyme activity **released** into the liquor within 3 minutes at 15° C. Exemplary granules that have been tested in support of the present invention exhibit an enzyme **release** rate of no less than 90% in 5 minutes at 15° C., and most exhibit an enzyme **release** rate of no less than 90% in 3 minutes at 15° C.

Summary Table

Granule Sample	Volumetric Density (g/ml)
Example. . .	

L57 ANSWER 26 OF 79 USPATFULL on STN (Continued)
enzymes.
SUM0 . . . more synthetic polymers or other excipients as known to those skilled in the art. Suitable synthetic polymers include polyethylene oxide, **polyvinyl** alcohol, **polyvinyl** pyrrolidone, polyethylene glycol and polyethylene oxide/polypropylene oxide.
SUM0 [0036] Suitable coatings include water soluble or water dispersible film-forming polymers such as **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, acrylic acid, xanthan, **carrageenan**, chitosan, latexs polymers, and enteric **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.
SUM0 . . . Preferably, the outer coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVA-methylmethacrylate copolymer and PVP-PVA copolymer.
DETD . . . cosmetically coated with 92.6 kg of an aqueous solution containing 7.1 kg (6.2% w/w) titanium dioxide, 2.9 kg (2.5% w/w) **methylcellulose**, 2.9 kg (2.5%) Pureone B790, 1.2 kg (1.5% w/w) Neodol 23/6.5, and 2.0 kg (1.67% w/w) of polyethylene glycol at . . .
CLM What is claimed is:
6. The granule of claim 3, wherein the coating is selected from the group consisting of **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan and carrageenan.

L57 ANSWER 27 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2002:123202 USPATFULL
TITLE: Lubricious coatings for substrates
INVENTOR(S): Burrell, Robert Edward, Sherwood Park, CANADA
Yin, Hua Qing, Sherwood Park, CANADA
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Theodore Nicholas, Walter Carlton, Edmonton, CANADA
Bowlby, Leonard Salvin, Sherwood Park, CANADA
Field, David James, Edmonton, CANADA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20020122265	A1	20021205
	US 6723350	B2	20040420
APPLICATION INFO.:	US 2002-173513	A1	20020423 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2001-840637, filed on 23 Apr 2001, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-285848	20010423 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	GREENLEE WINNER AND SULLIVAN P C, 5370 MANHATTAN CIRCLE, SUITE 201, BOULDER, CO, 80303	
NUMBER OF CLAIMS:	65	
EXEMPLARY CLAIM:	1	
LINE COUNT:	3141	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides methods and kits to form water swellable gel coatings, preferably lubricious coatings, on substrates, and coated substrates thus formed. The coatings contain one or more antimicrobial metals formed with atomic disorder, together with one or more antimicrobial metals formed with atomic disorder such that the coatings provide an antimicrobial and anti-inflammatory effect when wet. The invention also provides a method to produce metal powders by sputtering a coating onto a moving surface, and then scraping the coating with one or more scrapers to produce the metal powders. The method is particularly
useful for producing large amounts of nanocrystalline antimicrobial metal powders formed with atomic disorder, useful in the water swellable
gel coatings of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUM0 [0013] The lubricious polymer is preferably a hydrophilic polymer in powder form, most preferably one or more of carboxymethyl **cellulose**, **polyvinyl** alcohol and alginate. The antimicrobial metal is preferably one or more of *Ag, Au, Pd* or Pt (most preferably *Ag*). . . .
SUM0 [0030] "**Pharmaceutically**- or therapeutically-acceptable" is used herein to denote a substance which does not significantly interfere with
the effectiveness or the biological. . .
SUM0 [0043] The substrate may be formed of virtually any material, including polyurethane, **polyvinylchloride**, other vinyl polymers, polycarbonate, polystyrene, nylon, polyesters and polyacrylates, polypropylene, polybutylene, tetrafluoroethylene, **polyvinylacetal**, elastomers, latex

L57 ANSWER 27 OF 79 USPATFULL on STN (Continued)

rubber, rubber, silicone, other plastic, metal, glass, and composites.

SUMM . . . when dry. Such polymers are well known in the art. Preferred are hydrophilic polymers, including sodium, potassium and calcium alginates, **carboxymethylcellulose**, agar, gelatin, **polyvinyl** alcohol, collagen, pectin, chitin, chitosan, polyamino acids, polyesters, polylactic, poly-L-caprolactone, **polyvinylpyrrolidone**, polyethylene oxide, **polyvinyl** alcohol, polyether, polysaccharide, hydrophilic polyurethane, polyhydroxyacrylate, polymethacrylate, dextran, xanthan, hydroxypropyl **cellulose**, methyl **cellulose**, and homopolymers and copolymers of N-vinylpyrrolidone, N-vinylactam, N-vinyl butyrolactam, N-vinyl caprolactam, other vinyl compounds having polar pendant groups, acrylate and.

SUMM [0046] Most preferred lubricious polymers include hydrocolloid powders such as sodium, potassium and calcium alginates, **polyvinyl** alcohol, and **carboxymethylcellulose**. Other preferred lubricious polymers are **cellulose** and derivatives thereof, starch, glycogen, gelatin, pectin, chitosan, chitin, collagen, gum arabic, locust bean gun, karaya gun, gum

tragacanth, ghatti. . .

SUMM . . . as epidermal growth factor, platelet derived growth factor, transforming growth factor and interleukins, and bone morphogenetic proteins, and the like. **Polyvinyl** alcohol is a particularly preferred polymer and also acts as a texturing agent, methyl or propyl parabens are particularly preferred. . . .

SUMM . . . to deleteriously affect the lubricity, the antimicrobial effect

or the anti-inflammatory activity. Ingredients are thus only included in

therapeutically or **pharmaceutically** acceptable amounts. Ingredients to be avoided or limited in the coatings of the present invention, preferably to less than 0.01.

DETD [0028] A gel was made using carboxymethyl **cellulose** (2%), **polyvinyl** alcohol (0.5%), methyl paraben (0.1%), propyl paraben (0.02%), nanocrystalline silver powder of Example 1 (0.1%) and water (all amounts

in. . .

DETD [0059] A gel was made using carboxymethyl **cellulose** (2%), nanocrystalline silver powder of Example 1 (0.1 %) and water. After making the gel well, to distribute the nanocrystalline.

DETD [0074] Ex. 1--A commercial carboxymethyl **cellulose**/pectin gel (Duoderm®, Convatec) was combined with nanocrystalline silver powder prepared as set forth in Example 1 to produce a gel. . .

DETD [0095] Ex. 2--Carboxymethyl **cellulose** (CMC) fibers were coated directly to produce an atomic disordered nanocrystalline silver coating,

using magnetron sputtering conditions similar to those. . .

CLM What is claimed is:

5. The method of claim 4, wherein the lubricious polymer is one or more of **cellulose** and derivatives thereof, **polyvinyl** alcohol, starch, glycogen, gelatin, pectin, alginate, chitosan, chitin, gun arabic, locust bean gun, karaya gun, gum tragacanth, ghatti gum, agar-agar,. .

CLM What is claimed is:

6. The method of claim 4, wherein the lubricious polymer is selected

L57 ANSWER 27 OF 79 USPATFULL on STN (Continued)

from one or more of carboxymethyl **cellulose**, **polyvinyl** alcohol, and alginate.

CLM What is claimed is:

. . . 25. The method of claim 22, wherein the coating includes one or more agents selected from methyl paraben, propyl paraben, **polyvinyl** alcohol, heparin, β-glucan, epidermal growth factor, platelet derived growth factor, and transforming growth factor, in a therapeutically acceptable amount.

CLM What is claimed is:

32. The coated substrate of claim 31, wherein the lubricious polymer is one or more of **cellulose** and derivatives thereof, **polyvinyl** alcohol, starch, glycogen, gelatin, pectin, alginate, chitosan, chitin, gun arabic, locust bean gun, karaya gun, gum tragacanth, ghatti gun, agar-agar,. . .

CLM What is claimed is:

33. The coated substrate of claim 31, wherein the lubricious polymer is selected from one or more of carboxymethyl **cellulose**, **polyvinyl** alcohol, and alginate.

CLM What is claimed is:

. . . The coated substrate of claim 46, wherein the coating includes one or

more agents selected from methyl paraben, propyl paraben, **polyvinyl** alcohol, heparin, β-glucan, epidermal growth factor, platelet derived growth factor, and transforming growth factor, in a therapeutically acceptable amount.

CLM What is claimed is:

56. The kit of claim 55, wherein the lubricious polymer is one or more of **cellulose** and derivatives thereof, **polyvinyl** alcohol, starch, glycogen, gelatin, pectin, alginate, chitosan, chitin, gun arabic, locust bean gun, karaya gun, gum tragacanth, ghatti gun, agar-agar,.

CLM What is claimed is:

57. The kit of claim 55, wherein the lubricious polymer is selected from

one or more of carboxymethyl **cellulose**, **polyvinyl** alcohol, and alginate.

IT 1398-61-4, Chitin 7440-22-4, Silver, biological studies 9000-01-5, Gun arabic **9000-07-1**, Carrageenan 9000-28-6, Ghatti gum 9000-30-0, Guar gum 9000-34-5, Karaya gum 9000-40-2, Locust bean gum 9000-65-1, Gum tragacanth 9000-69-5, Pectin 9002-18-0, Agar agar 9002-89-5 9004-32-4, Cm **cellulose** 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9001-79-2, Glycogen, biological studies 9013-76-4, Chitosan 11138-66-2, Xanthan gum (lubricious **coatings** containing nanocryst. silver and polymers for medical surfaces)

IT **9000-07-1**, Carrageenan

(lubricious **coatings** containing nanocryst. silver and polymers for medical surfaces)

L57 ANSWER 28 OF 79 USPATFULL on STN

ACCESSION NUMBER: 2002:197307 USPATFULL

TITLE: **Pharmaceutical** formulations for acid labile substances

INVENTOR(S): Odidi, Ima, 2136 Opal Court, Mississauga, Ontario, L5K 2S5, CANADA
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	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6479075	B1	20021112	
APPLICATION INFO.:	US 2001-767028		20010122 (9)	<--
RELATED APPLN. INFO.: Oct	Continuation of Ser. No. US 1998-166274, filed on 5			
	1998, now patented, Pat. No. US 6296876			

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1997-61211P	19971006 (60)	<--
	US 1997-68917P	19971222 (60)	<--
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Spear, James M.		
LEGAL REPRESENTATIVE:	Clauss, Isabelle M., Foley Hoag LLP		
NUMBER OF CLAIMS:	15		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)		
LINE COUNT:	512		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention in general relates to novel **pharmaceutical** compositions for acid labile substances as well as for methods of making such. Specifically, the invention provides a **pharmaceutical** composition comprising about 1 to 75% by weight acid labile compound, up to about 5%

by weight disintegrant, at least one protector coat layer used to separate and protect the acid labile substance from acid reacting groups

and gastric juice, and at least one enteric coat layer which surrounds the protector coating layer and ensures delivery of over 80% the acid labile substance to the small intestine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI **Pharmaceutical** formulations for acid labile substances

AB This invention in general relates to novel **pharmaceutical** compositions for acid labile substances as well as for methods of making such. Specifically, the invention provides a **pharmaceutical** composition comprising about 1 to 75% by weight acid labile compound, up to about 5%

by weight disintegrant, at least. . .

SUMM This invention in general relates to novel **pharmaceutical** compositions for acid labile substances as well as for methods of making such.

SUMM In order to provide a **pharmaceutical** composition containing such acid labile substances which is not degraded in the gastrointestinal tract, the acid labile substances must be enteric coated. However, **pharmaceutically** acceptable enteric coating materials are acidic in nature or contain acid reacting groups. Therefore, if the acid labile substances are. . .

L57 ANSWER 28 OF 79 USPATFULL on STN (Continued)
SUM04 U.S. Pat. Nos. 4,853,230 and 5,784,935 describe enteric coated **pharmaceutical** formulations of acid labile substances for oral use, where the cores contain acid labile drugs mixed with alkaline reacting substances. . .
SUM05 U.S. Pat. No. 2,540,797 describes an enteric coated **pharmaceutical** in an oral dosage form, where the enteric coating is combined with a second and/or first coating of water insoluble. . .
SUM06 WO No. 85/03436 discloses a **pharmaceutical** preparation in which the core contains active drugs mixed with buffering compounds such as sodium dihydroorgenphosphate which maintains a constant pH. A coating material is used to provide a constant rate of diffusion of the **pharmaceutical** active. However, this formulation is not suitable for acid labile compounds where a rapid **release** in the small intestine is required. The direct application of an enteric coating onto the **pharmaceutical** active would adversely influence the storage stability of the acid labile compounds contained therein.
SUM07 DE-A1 1 204 363 describes a time layer coating method for **pharmaceuticals**. The first coating layer is a surface membrane soluble in gastric but insoluble in intestinal juice. The second coating layer. . . coating. This method is complicated and is also not suitable for acid labile compounds such as substituted benzimidazoles where rapid **release** of the drug in the small intestine is required, as it results in a dosage form which is not dissolved. . . .
SUM08 There wis therefore a need to develop a **pharmaceutical** composition for acid labile substances that adequately protected the acid labile active prior to its being **released** in the small intestine. Accordingly, a novel **pharmaceutical** composition was developed for the delivery of acid labile substances to the gut which differs form known compositions and delivery. . . enteric coating composition(s) used in the composition. These lead to a different mechanism by which the acid labile drug is **released** in the small intestine to provide a stabilised acid labile compound composition.
SUM09 The novel **pharmaceutical** composition comprises an acid labile compound or an alkaline salt of the labile compound. The composition optionally comprises acid sequestering agent(s).
SUM10 According to an object of the present invention there is provided a **pharmaceutical** composition comprising:
SUM11 According to another object of the present invention is a method for preparing the novel **pharmaceutical** composition of the present invention.
SUM12 The novel **pharmaceutical** composition is well suited for oral administration in a dosage unit form.
DET . . . substances for use in the composition of the present invention include but are not limited to aminoalkyl methacrylate copolymers and **ethylcellulose**. Most preferably is Eudragit E, a cationic copolymer based on dimethylaminoethyl methacrylate and neutral methacrylates. The acid sequestering compound may also be mixed with inert **pharmaceutical** fille(s) such as lactose, starch and microcrystalline **cellulose**.
DET . . . Preferably, 2 to 5% by weight disintegrants are incorporated into the composition. The disintegrants may be optionally mixed with

L57 ANSWER 28 OF 79 USPATFULL on STN (Continued)
. . . **pharmaceutical** techniques. After forming they are first coated with the protective coat(s) and then with the enteric coat as previously described.
DET . . . storage. The final composition of the present invention provides that not more than 10% of the acid labile substance is **released** in said media in about 2 hours and more than about 80% of the acid labile substance is **released** in 24 hours in alkaline media using USP dissolution apparatus I, II, III and IV.
DET Methods of synthetic chemistry, physical and **pharmacology** referred to but not explicitly described in this disclosure and examples are reported in the scientific literature are well known. . .
DET

Omeprazole 20 mg
Eudragit E 20 mg
Lactose 80 mg
Calcium sulfate dihydrate 20 mg
Carboxymethylcellulose sodium 20 mg
Microcrystalline **cellulose** 20 mg
Sodium lauryl sulfate 20 mg
PVP XL.10 4 mg
Talc 10 mg
DET Lactose, microcrystalline **cellulose**, sodium lauryl sulfate, **carboxymethylcellulose** sodium, and calcium sulfate dehydrate were blended in a planetary mixer. The blend was granulated with alcoholic solution of Eudragit. . .
DET . . . 3.00 kg
Eudragit E 0.900 kg
Keelin 0.100 kg
Talc 0.090 kg
Acetone 0.234 kg
Isopropyl alcohol 0.281 kg
Ethylcellulose 2% salin 0.900 kg
DET . . . propeller mixer. Apply the protector coat solution unto the tablets in a perforated coating pan. Apply a 1-3% solution of **ethylcellulose** to the protector coated tablets in a perforated coating pan. . . .
DET . . . 20 mg
Eudragit E 20 mg
Lactose 80 mg
Calcium sulfate dihydrate 20 mg
Sodium lauryl sulfate 20 mg
Microcrystalline **cellulose** 20 mg
Sodium starch glycolate 5 mg
Talc 15 mg
DET Lactose, microcrystalline **cellulose**, calcium sulfate and sodium lauryl sulphate were blended in a planetary mixer. The blend was granulated with alcoholic solution of. . .
DET

Protector coated tablets from II 3.450 kg
Hydroxypropyl **methylcellulose** acetate succinate** 0.345 kg

**from the following coating solution shown below for 3 kg batch
DET

Hydroxypropyl **methylcellulose** acetate succinate 0.345 kg
Triethyl citrate 0.041 kg

L57 ANSWER 28 OF 79 USPATFULL on STN (Continued)
. . . ieryl **pharmaceutical** fillers such as lactose, calcium sulfate and microcrystalline, **cellulose**.
DET . . . the core of the composition. The core is then coated with a protector coat of an acid sequestering substance and/or **ethylcellulose** optionally containing one or more **pharmaceutical** excipients such as kaolin, bentonite and talc and further enteric coated with an enteric coating polymer such as, for example, shellac or hydroxypropyl **methylcellulose** acetate succinate which allows the dissolution of the coating in the proximal section of the small intestine. It may also. . . due to swelling and liquid wicking action of the disintegrant such as methacrylic acid DVP, pregelatinized starch, cross linked carboxymethyl **cellulose**, cross linked starch, or cross linked **polyvinyl** pyrolidone present in the cores.
DET . . . with one or more layers of an acid sequesting compound such as the aminoalkyl methacrylate copolymers, preferably Eudrigit E and/or **ethylcellulose**, optionally containing one or more **pharmaceutical** excipients. This "protector coat" is also acts as a barrier to and reacting groups from reaching the core containing acid labile compound(s). The protector coat is applied as one or more layers optionally containing one or more **pharmaceutical** excipient such as plasticizers, pigment and anti-sticking agents. The protector coat is applied using either aqueous or solvent based pan, . . . thickness of the protector layer(s) is not less than 0.001 mg/cm.sup.2 and the amount of acid sequestering compound and or **ethylcellulose** is not less than 0.1% but preferably 0.5-10% respectively. One example of a preferred protector coat is that of a. . .
DET The final composition can be made into pellets or pressed into tablets using conventional **pharmaceutical** processes. The pellets or tables can be used as cores or placed in gelatin capsules and used as cores.
DET . . . their derivatives. Another example of a preferred enteric coating polymer is the acetic and mono succinic acid ester of hydroxypropyl **methylcellulose** preferably hydroxypropyl **methylcellulose** acetate succinate, having free succinic acid not more than 30% preferably not more than 14 and weight-average molecular weight 4.5 to 12×10.sup.-4 daltons measured by gel permeation chromatography. Other suitable members of the enteric **cellulose** esters are **cellulose** acetate phthalate (**cellulose** acetate trimellitate and hydroxypropyl **methylcellulose** phthalate. Enteric coating of the type methacrylic acid copolymers can also be used. Further examples of suitable enteric coating polymers. . . . A ce type S or type C, or any combination thereof. These enteric coating polymer optionally contain one or more **pharmaceutical** excipients such as plasticizer(s), pigment(s) and colorant. Both protector and enteric coats can be applied from either aqueous, organic or. . .
DET . . . above forms another aspect of the embodiment of this invention.
. . . The acid sequestering compound is used to granulate the chosen **pharmaceutical** fillers using a fluidized bed technique, high shear granulator, blender or planetary mixer. The granulating liquid can be either aqueous. .
DET The granules are formed into pellets or tablets using conventional

L57 ANSWER 28 OF 79 USPATFULL on STN (Continued)
Ethanol/water (80:20) 0.807 kg
Pigment suspension 0.034 kg
Opadry
Talc 0.034 kg
. . .
DET

Omeprazole 20 mg
Lactose 115 mg
Sodium lauryl sulfate 25 mg
Microcrystalline **cellulose** 20 mg
Sodium starch glycolate 5 mg
Talc 15 mg
DET Lactose, microcrystalline **cellulose** and sodium lauryl sulphate were blended in a planetary mixer. The blend was granulated with alcoholic solution and dried in. . . .
DET . . . 3.0 kg
Eudragit E 0.3 kg
Kaolin 0.10 kg
Talc 0.05 kg
Acetone 0.234 kg
Isopropyl alcohol 0.281 kg
Ethylcellulose 2% 1.500 kg
DET Apply a 2% solution of **ethylcellulose** to the tablets for I in a perforated coating pan. Finely disperse kaolin and Talc in the Eudragit E solvent mixture using a propeller mixer. Apply this solution unto the **ethylcellulose** coated tablets in a perforated coating pan.
DET

Protector coated tablets from II 3.450 kg
Hydroxypropyl **methylcellulose** acetate succinate 0.345 kg
DET

Hydroxypropyl **methylcellulose** acetate succinate 0.345 kg
Triethyl citrate 0.041 kg
Ethanol/water (80:20) 0.807 kg
Pigment suspension
Opadry 0.034 kg
Talc 0.034 kg
. . .
DET

Omeprazole 20 mg
Lactose 90 mg
Microcrystalline **cellulose** 30 mg
Calcium sulfate 30 mg
Sodium lauryl sulphate 20 mg
PVP XL.10 4 mg
Talc 15 mg
DET Lactose, microcrystalline **cellulose**, calcium sulfate, sodium lauryl sulfate and omeprazole were blended in a planetary mixer. The blend was granulated with alcoholic solution. . .
DET

Protector coated tablets from II 3.000 kg
Hydroxypropyl **methylcellulose** acetate succina 0.50 kg
Talc 0.045 kg
Triethyl citrate 0.042

L57 ANSWER 28 OF 79 USPATFULL on STN (Continued)
Sodium lauryl sulphate 0.025
DETD

Omeprazole 20 mg
Lactose 75 mg
Microcrystalline **cellulose** 40 mg
Calcium sulphate 30 mg
Sodium lauryl sulphate 20 mg
Talc 15 mg
DETD Lactose, microcrystalline **cellulose**, calcium sulfate, sodium lauryl sulfate and omeprazole were blended in a planetary mixer. The homogeneous blend was blended with talc. . .

DETD

Protector coated pellets/tablets from II 3.450 kg
Hydroxypropyl **methylcellulose** acetate succinate** 0.345 kg

**from the following coating solution shown below for 3 kg batch
DETD

Hydroxypropyl **methylcellulose** acetate succinate 0.345 kg
Triethyl citrate 0.041 kg
Ethanol/water (80:20) 2.907 kg
Pigment suspension
Opadry 0.224 kg
Talc 0.034 kg
. . .
DETD

Omeprazole 20 mg
Lactose 100 mg
Calcium sulfate 30 mg
Sodium lauryl sulphate 20 mg
Microcrystalline **cellulose** 15 mg
Sodium starch glycolate 30 mg
Talc 5 mg
DETD Lactose, microcrystalline **cellulose**, omeprazole, sodium lauryl sulfate, calcium sulfate and corn starch were blended in a planetary mixer. The blend was granulated with. . .

DETD

Protector coated pellets/tablets from II 3.450 kg
Hydroxypropyl **methylcellulose** acetate succinate** 0.345 kg

**from the following coating solution shown below for 3 kg batch
DETD

Hydroxypropyl **methylcellulose** acetate succinate 0.345 kg
Triethyl citrate 0.041 kg
Ethanol/water (80:20) 2.907 kg
Pigment suspension
Opadry 0.224 kg
Talc 0.034 kg
. . .

L57 ANSWER 29 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2002122807 USPATFULL
TITLE: Edible FGA coating composition
INVENTOR(S): Augello, Michael, Marlboro, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20020121225	A1	20020905
	US 6932981	B2	20050823
APPLICATION INFO.:	US 2002-77338	A1	20020215 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2001-994252, filed on 26 Nov 2001, PENDING		

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-284778P	20010419 (60)	<--
	US 2001-268609P	20010214 (60)	<--
	US 2000-253445P	20001128 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FMC Corporation, Patent Administrator, 1735 Market Street, Philadelphia, PA, 19103
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
LINE COUNT: 807
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable coating composition is disclosed which comprises a high levels of low viscosity propylene glycol alginate and a surfactant, which may additionally contain a filler, a pigment, and optionally a small amount of a secondary film former and/or a strengthening polymer. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . and a secondary film former and/or a strengthening polymer. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

SUMM [0001] It is a common practice to coat **pharmaceutical** and veterinary tablets to obtain several advantages. Among these are to improve the surface characteristics of tablets to make them.

SUMM [0002] Another very important function of a **pharmaceutical** or veterinary tablet coating is to improve the integrity of the tablet itself. Uncoated tablets are often subject to being. . .

SUMM . . . proportion to the increase in disintegration time. Many other agents commonly used in coating compositions are also known to delay **release** of **pharmaceutical** agents, such as enteric coatings which use polymeric film forming materials which are insoluble in water, or gastric fluid, some of these being specifically selected to by-pass both the stomach and small intestine and provide colonic **release**.

SUMM [0038] The coatings of this invention meet U.S. **Pharmacopoeia**

L57 ANSWER 28 OF 79 USPATFULL on STN (Continued)
CLM What is claimed is:
1. A method for producing a **pharmaceutical** composition comprising an acid labile compound, said method comprising: combining doubt 1-75% by weight proton pump inhibitor compound and up. . .

CLM What is claimed is:
. . . method of claim 2, wherein said acid sequestering compound is selected from the group consisting of aminoalkyl methacrylate copolymer and **ethylcellulose**.

CLM What is claimed is:
4. The method of claim 3, wherein said acid sequestering compound is further admixed with inert **pharmaceutical** fillers selected from the group consisting of lactose, starch and microcrystalline **cellulose**.

CLM What is claimed is:
5. The method of claim 1, wherein said protective coat layer additionally comprises an inert **pharmaceutical** filler selected from the group consisting of lactose, starch and microcrystalline **cellulose**.

CLM What is claimed is:
6. The method of claim 5, wherein said protective coat layer additionally comprises a **pharmaceutical** excipient selected from the group consisting of plasticizers, pigment and anti-tacking agents.

CLM What is claimed is:
. . . selected from the group consisting of sodium starch glycolate, croqpovidone, pregelatinized starch, methacrylic acid DVB, croscarmellose sodium and cross-linked carboxymethyl **cellulose**.

CLM What is claimed is:
8. The method of claim 7, wherein said disintegrant is additionally mixed with an inert **pharmaceutical** filler selected from the group consisting of lactose, calcium sulfate and microcrystalline **cellulose**.

CLM What is claimed is:
13. The method of claim 10, wherein said enteric coating is selected from the group consisting of shellac, constituent aliphatic polyhydroxy acids of shellac, acetic and mono succinic acid esters of hydroxypropyl **methylcellulose**, and methacrylic acid copolymers.

CLM What is claimed is:
14. The method of claim 12, wherein said enteric coating additionally comprises a **pharmaceutical** excipient selected from the group consisting of plasticizers, pigments and colorants.

CLM What is claimed is:
15. The method of claim 1, wherein said protective **coating** comprises **carrageenan** or nonionic polyethylene oxide polymers having a molecular weight of over 20,000 daltons.

L57 ANSWER 29 OF 79 USPATFULL on STN (Continued)
standards for rapid or immediate dissolution (U.S.P. monograph 23) of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates. Thus, they do not adversely impact or retard **release** of active ingredients from a substrate coated with them. Further, the coatings of this invention are readily dispersed and rapidly. . . .

SUMM . . . a secondary film former and/or a strengthening polymer as an additional ingredient. More specifically, the present invention provides a prompt **release**, edible, hardenable FGA coating composition, as well as dry coatings and aqueous dispersions thereof and solid dosage forms coated therewith.

SUMM [0012] For purposes of this application, the term "edible" is intended to mean food or **pharmaceutical** grade materials which are approved by regulatory authorities for use in **pharmaceutical** or food applications. The term "hardenable," used to describe the coating formulations of this invention, is intended to include only. . . this invention or tablets coated with the compositions of this invention, mean that the coatings of this invention meet U.S. **Pharmacopoeia** standards (U.S.P. monograph 23) for rapid or immediate dissolution of active ingredient from tablets or other solid dosage forms coated with them. Thus, they provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates. They do not, when placed in water or ingested, adversely impact or retard **release** or dissolution of tablets or other dosage forms coated with them. Coatings made in accordance with the present invention are. . .

SUMM . . . glycol alginate provides important film-forming characteristics required to provide an elegant coating which is particularly useful in, for example, coating **pharmaceutical** and veterinary tablets, caplets, granules, and spheres which contain active ingredients which require **release** promptly after being placed in solution or ingested.

SUMM . . . may include a minor amount of secondary film former such as carrageenan or HPMC and/or a strengthening polymer such as **hydroxyethylcellulose**.

SUMM . . . example, dicalcium carbonate, dicalcium phosphate and carbohydrates, such as starch, maltodextrin, lactose, mannitol and other sugars, croscarmellose sodium, or microcrystalline **cellulose**. Of these, maltodextrin has been found beneficial at about 20% to about 30% by dry weight of the composition, but. . .

SUMM . . . formulation, it may be desirable to include a secondary film former such as carrageenan and/or a strengthening polymer such as **hydroxyethylcellulose**. While such additional additives are generally not required, they may be utilized if desired at about 3% to about 12%.

SUMM . . . dry weight of the composition of a secondary film forming polymer such as carrageenan or a strengthening polymer such as **hydroxyethylcellulose**. Preservatives, such as methyl paraben at 0.75% to 1.50% and/or propyl paraben at 0.075% to 0.15% may also be present. . .

SUMM . . . may be preferable to maintain agitation of the aqueous

L57 ANSWER 29 OF 79 USPATFULL on STN (Continued)

dispersion during the entire period of its being sprayed onto the **pharmaceutical** or veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizer, pesticide tablets, or food.

SUMM [0023] The preferred edible, hardenable, prompt **release** coating formulations of this invention may generally be prepared and used according to a simple procedure. Propylene glycol alginate and. . . .

SUMM . . . thixotropic behavior of a formulation which sets up during overnight storage. Unlike coating formulations based primarily on hydroxyalkyl ethers of **cellulose**, for example, HPMC, constant stirring of the propylene glycol alginate-based formulations of this invention does not need to be continued. . . .

SUMM [0026] The level of coating applied on a **pharmaceutical** or veterinary dosage form is preferably between about 0.5% to about 4% by weight of the uncoated dosage form, more. . . .

SUMM [0029] All components of the formulation are typically **pharmaceutically** acceptable, edible food grade materials.

DETD . . . twin shell blender were placed 292 grams of low viscosity propylene glycol alginate (Profarm, Pronova/FMC Corporation) and 65 grams of **hydroxyethylcellulose** 250 L, 22.5 grams of hydroxylated soy lecithin (Precept 8103, Central Soya), 45 grams of maltodextrin M1 80 (Maltrin M1. . .

DETD . . . 55

Lecithin.sup.2	3.3	5	7	5	2.5	5	
Maltodextrin.sup.3	--	10	18	30	30	25	
Pigment	13.4	10	10	--	7.5	10	
WAC.sup.4	--	**10**	--	--	--	--	
Soft **carrageenan**	--	--	--	--	--	5	
Caplet Ingredients							
Acetaminophen					X	X	
Ibuprofen	X	X	X	X			
Chlorpheniramine				X			
Coating Weight (%)	3	3	3	3	3	3	
Friability. . .	minutes		92	91			
6Q minutes		99	99				

.sup.1Polypropylene glycol alginate (Profarm **S**, Pronova/FMC Corporation)
.sup.2Hydroxylated soy lecithin, Central Soya
.sup.3Maltodextrin, Maltrin M180
.sup.4**Hydroxyethylcellulose** WAC
.sup.5% = excellent; 4 = acceptable; 3 = marginal; 2 = poor; 1 = Not acceptable
.sup.6Not tested

CLM What is claimed is:
1. An edible, hardenable, prompt **release** coating composition comprising 35% to 100% of propylene glycol alginate and up to 10% of a surfactant, wherein the propylene.

CLM What is claimed is:
11. The **coating** composition of claim **10** wherein **carrageenan** is present at 5% to 20% by dry weight of the composition.

CLM What is claimed is:
12. The coating composition of claim 10 where **hydroxyethylcellulose** is present at 5% to 30% by dry weight of the composition.

L57 ANSWER 30 OF 79 USPATFULL on STN

ACCESSION NUMBER:	2002:125963 USPATFULL
TITLE:	Edible FGA coating composition
INVENTOR(S):	Aspelin, Michael, Hillsboro, NJ, UNITED STATES Billefernich, Eric, Yardville, NJ, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 20020058633	A1	20020815	
	US 6899935	B2	20040502	
APPLICATION INFO.:	US 2001-994252 A1	20011126 (9)		
	NUMBER		DATE	
PRIORITY INFORMATION:	US 2001-284778P		20010419 (60)	<--
	US 2001-285224P		20010404 (60)	<--
	US 2000-253406P		20001128 (60)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	APPLICATION			
LEGAL REPRESENTATIVE:	Patent Administrator, FMC Corporation, 1735 Market Street, Philadelphia, PA, 19103			
NUMBER OF CLAIMS:	19			
EXEMPLARY CLAIM:	1			
LINE COUNT:	669			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable coating composition is disclosed which comprises high levels of low viscosity propylene glycol alginate and a surfactant, which may additionally contain a filler, a pigment, and optionally a small amount of a secondary film former and/or a strengthening polymer. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, **seeds**, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . of a secondary film former and/or a strengthening polymer. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

SUMM [0001] This invention relates to edible, hardenable prompt **release** coating compositions comprising a film forming amount of low viscosity propylene glycol alginate that serves as the principle, primary or sole film former of the coating composition. The coatings of the present invention can be applied to **pharmaceutical**, including nutraceutical, and veterinary solid dosage forms, such solid substrates such as seeds, animal feed, fertilizers, pesticide tablets and granules. . . . dispersed in aqueous media, and, when applied as a coating, provide high lustre coatings which do not retard or extend **release** of active ingredient from a coated substrate.

SUMM [0002] It is a common practice to coat **pharmaceutical** and veterinary tablets to obtain several advantages. Among these are to improve the surface characteristics of tablets to make them.

SUMM [0003] Another very important function of a **pharmaceutical** or veterinary tablet coating is to improve the integrity of the tablet itself. Uncoated tablets are often subject to being. . . .

SUMM . . . proportion to the increase in disintegration time. Many other agents commonly used in coating compositions are also known to delay **release** of **pharmaceutical** agents, such as enteric coatings which use polymeric film forming materials which are insoluble in water, or gastric fluid, some of these being specifically selected to by-pass both the stomach and small intestine and provide colonic **release**.

SUMM [0011] The coatings of this invention meet U.S. **Pharmacopoeia** standards for rapid or immediate dissolution (U.S.P. monograph 23) of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates. Thus, they do not adversely impact or retard **release** of active ingredients from a substrate coated with them. Further, the coatings of this invention are readily dispersed and rapidly . . .

SUMM . . . a secondary film former and/or a strengthening polymer as an additional ingredient. More specifically, the present invention provides a prompt **release**, edible, hardenable FGA coating composition, as well as dry coatings and aqueous dispersions thereof and solid dosage forms coated therewith.

SUMM [0013] For purposes of this application, the term "edible" is intended to mean food or **pharmaceutical** grade materials which are approved by regulatory authorities for use in **pharmaceutical** or food applications. The term "hardenable," used to describe the coating compositions of this invention, is intended to include only. . . . this invention or tablets coated with the compositions of this invention, mean that the coatings of this invention meet U.S. **Pharmacopoeia** standards (U.S.P. monograph 23) for rapid or immediate dissolution of active ingredients from tablets or other solid dosage forms coated with them. Thus, they provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates. They do not, when placed in water or ingested, adversely impact or retard **release** or dissolution of tablets or other dosage forms coated with them. Coatings made in accordance with the present invention are . . . glycol alginate, provides important film-forming characteristics required to provide an elegant coating which is particularly useful in, for example, coating **pharmaceutical** and veterinary tablets, caplets, granules, and spheres which contain active ingredients which require **release** promptly after being placed in aqueous media or ingested.

SUMM . . . may include a minor amount of secondary film former such as carrageenan or HPMC and/or a strengthening polymer such as **hydroxyethylcellulose**.

SUMM . . . example, calcium carbonate, dicalcium phosphate and carbohydrates, such as starch, maltodextrin, lactose, mannitol and other sugars, croscarmellose sodium, or microcrystallins **cellulose**. Of these, maltodextrin has been found beneficial at about 10% to about 30% by dry weight of the composition, but. . .

SUMM . . . formulation, it may be desirable to include a secondary film

L57 ANSWER 30 OF 79 USPATFULL on STN (Continued)
form; such as carrageenan and/or a strengthening polymer such as **hydroxyethylcellulose**. While such additional additives are generally not required, they may be utilized if desired at about 2% to about 12%. . . .

SUMM . . . dry weight of the composition of a secondary film forming polymer such as carrageenan or a strengthening polymer such as **hydroxyethylcellulose**. Preservatives, such as methyl paraben at 0.75% to 0.50% and/or propyl paraben at 0.075% to 0.25% may also be present. . . .

SUMM . . . may be preferable to maintain agitation of the aqueous dispersion during the entire period of its being sprayed onto the **pharmaceutical** or veterinary solid dosage form, confectionery, seeds, animal feed, fertilizer, pesticide tablets, or food.

SUMM [0024] The preferred edible, hardenable, prompt **release** coating formulations of this invention may generally be prepared and used according to a simple procedure. Propylene glycol alginate and. . .

SUMM . . . thixotropic behavior of a formulation which sets up during overnight storage. Unlike wanting formulations based primarily on hydroxylaly; ethers of **cellulose**, for example, HPMC, constant stirring of the propylene glycol alginate-based formulations of this invention does not need to be continued.

SUMM [0027] The level of coating applied to **pharmaceutical** or veterinary dosage forms is preferably between about 0.5% to about 4% by weight of the uncoated dosage form, more. . .

SUMM [0030] All components of the formulation are typically **pharmaceutically** acceptable, edible food grade materials.

DETD . . . twin shell blender were placed 292 grams of low viscosity propylene glycol alginate (Profoam, Provova/FMC Corporation) and 65 grams of **hydroxyethylcellulose** 250L, 22.5 grams of hydroxylated soy lecithin (Precept 8106, Central Soya), 45 grams of maltodextrin M1 9G (Maltrin M1 9G, . . .

DETD							
Lecithin.sup.2	3.3	5	7	5	2.5	5	
Maltodextrin.sup.3	--	10	10	30	30	25	
Pigment	13.4	10	10	--	7.5	10	
HEC.sup.4	--	10	--	--	--	--	
Iota **carrageenan**	--	--	--	--	--	5	
Caplet Ingredients							
Acetaminophen					X	X	
Chlorpheniramine	X	X	X				
Coating Weight (%)	3	3	3	3	3	3	
Friability . . . minutes				92	91		
60 minutes		99	99				

.sup.1Polypropylene glycol alginate (Profoam ®, Provova/FMC Corporation)
.sup.2Hydroxylated soy lecithin, Central Soya
.sup.3Maltodextrin, Maltrin M180
.sup.4**Hydroxyethylcellulose** 250L
.sup.5S = excellent; 4 = acceptable; 3 = marginal; 2 = poor; 1 = Not acceptable
.sup.6Not tested
CLM What is claimed is:

L57 ANSWER 31 OF 79 USPATFULL on STN (Continued)
1. An edible, hardenable, prompt **release** coating composition comprising 55% to 90% of propylene glycol alginate and 2% to 10% of a surfactant, wherein the propylene.

CLM What is claimed is:
10. The **coating** composition of claim 9 wherein **carrageenan** is present at 5% to 30% by dry weight of the composition.

CLM What is claimed is:
11. The coating composition of claim 9 where **hydroxyethylcellulose** is present at 5% to 30% by dry weight of the composition.

L57 ANSWER 32 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2002:251684 USPATFULL
TITLE: Edible coating composition
INVENTOR(S): Augello, Michael, Matlboro, NJ, United States
Dell, Sheila M., New Hope, PA, United States
Thaker, Domingo C., Bensalem, PA, United States
Modliszewski, James J., Brick, NJ, United States
Stanley, Thomas A., Rockaway, NJ, United States
Werner, David E., West Grove, PA, United States
PATENT ASSIGNEE(S): FMC Corporation, Philadelphia, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6452469	B1	20020917	
APPLICATION INFO.:	US 2000-691724		20001017 (9)	<--

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-159059P	19990928 (60)	<--
	US 1999-162514P	19991029 (60)	<--
	US 1999-139292P	19990507 (60)	<--
	US 1999-167407P	19991124 (60)	<--
	US 1999-172124P	19991217 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Pulliam, Amy E.
LEGAL REPRESENTATIVE: Woodcock, Washburn, Kurtz, Mackiewicz & Norris, LLP
NUMBER OF CLAIMS: 39
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 1350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable **coating** composition containing microcrystalline **cellulose** and **carrageenan** and either a strengthening polymer, a plasticizer or both. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage form, confectionery, seeds, animal feed, fertilizer, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable **coating** composition containing microcrystalline **cellulose** and **carrageenan** and either a strengthening polymer, a plasticizer or both. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage form, confectionery, seeds, animal feed, fertilizer, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

SUMM This invention relates to edible, hardenable, prompt **release coating** compositions comprising microcrystalline **cellulose**, **carrageenan** and at least one of a strengthening polymer or a plasticizer. The coatings of the present invention can be applied to **pharmaceutical**, including nutraceutical, and veterinary solid dosage forms, confectionery, seeds,

L57 ANSWER 32 OF 79 USPATFULL on STN (Continued)
animal feed, fertilizer, pesticide tablets and granules, and foods, are

readily. . . media, and, when applied as a coating and ingested by, for example, a human, do not significantly retard or extend **release** of active ingredient(s) from a substrate coated therewith.

SUMM It is a common practice to coat **pharmaceutical** and veterinary tablets to obtain several advantages. Among these are to mask unpleasant tasting

active ingredients with a barrier coat. . . .

SUMM Another very important function of a **pharmaceutical** or veterinary tablet coating is to improve the integrity of the tablet itself. Uncoated tablets are often subject to being.

SUMM Currently, most commercially available edible coatings utilize a synthetic **cellulosic** polymer such as **hydroxypropylmethylcellulose** (HPMC). Other synthetic film-formers which are commonly used include **ethylcellulose**, **methylcellulose**, **polyvinylpyrrolidone**, and polydextrose. These coating materials may be used alone or in combination with secondary film-formers such as sodium alginate or. . .

SUMM . . . proportion to the increase in disintegration time. Many other agents commonly used in coating compositions are also known to delay **release** of **pharmaceutical** agents, such as enteric coatings which use polymeric film formers materials which are insoluble in water, or gastric fluid, some of these being specifically selected to by-pass both

the stomach and small intestine and provide colonic **release**.

SUMM The coatings of this invention meet U.S. **Pharmacopeia** standards for rapid or immediate dissolution (U.S.P. monograph 23) of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or dissolution consistent with the **release** rates which are usually obtained with the uncoated tablets or other substrates. Thus, they do not adversely impact or retard **release** of active ingredients from a substrate coated with them. Further, the coatings of this invention are readily dispersed and rapidly. . . .

SUMM . . . with the present invention by a coating composition which comprises a unique combination of materials specifically adapted for a prompt **release** when placed aqueous media or ingested, e.g., by a human. The coating compositions of the present invention comprises microcrystalline **cellulose**, carrageenan, and at least one of a strengthening polymer and a plasticizer. More specifically, the present invention provides a prompt **release**, edible, hardenable **coating** composition comprising microcrystalline **cellulose** and **carrageenan**, and at least one of strengthening polymer or plasticizer, preferably both, as well as to dry coatings and aqueous dispersions. . . .

SUMM The present invention also provides **pharmaceutical**, including nutraceutical, and veterinary solid dosage forms, confectionary, seeds,

animal feed, fertilizer, pesticide tablets and granules, and foods coated with the prompt **release** edible, hardenable composition of this invention.

SUMM . . . application, the term "edible" is intended to mean food grade materials which are approved by regulatory authorities for use in **pharmaceutical** or food applications. The term "hardenable" used to describe the coating compositions of this invention is intended to include only. . . that can be handled and packaged but which do not resist abrasive forces significantly. The terms "immediate", "rapid" or "prompt" **release** as applied to dissolution rates or times for the coating compositions of this invention or tablets coated with the

L57 ANSWER 31 OF 79 USPATFULL on STN (Continued)
compositions of this invention mean that the coatings of this invention

meet U.S. **Pharmacopoeia** standards (U.S.P. monograph 23) for rapid or immediate dissolution of active ingredients from tablets or other solid dosage forms coated therewith. Thus, they provide prompt **release** or dissolution consistent with the **release** rates which are normally obtained with the uncoated tablets or other substrate. They do not, consistent with the **pharmacopoeia** standards above, when placed in aqueous media or ingested by, e.g., a human, significantly impact or retard **release** or dissolution of tablets or other solid dosage forms coated therewith. For example, coatings made in accordance with the present . . . completely disintegrated and/or dissolved within less than 30 minutes after being ingested or placed in aqueous media. Thus, when a **pharmaceutical** solid dose, or tablet is coated with the coating of this invention and ingested by a human or other animal, the . . .

SUMM The microcrystalline **cellulose**, or hot coprocessed with the carrageenan or simply blended therewith, interacts with the carrageenan to provide superior film-forming characteristics required to provide an adequate coating which is particularly useful in, for example, coating **pharmaceutical** and veterinary tablets, caplets, granules, and spheres which contain active ingredients which require **release** promptly after being placed in aqueous media or ingested.

SUMM Microcrystalline **cellulose** is a purified, partially depolymerized **cellulose** that is generally prepared from high quality alpha **cellulose**, preferably alpha **cellulose** in the form of a pulp from fibrous plants, with a mineral acid, preferably hydrochloric acid. The acid selectively attacks the less ordered regions of the **cellulose** polymer chain, thereby exposing and freeing the crystalline regions, forming the crystallite aggregates which constitute microcrystalline **cellulose**. These are then separated from the reaction mixture and washed to remove degraded by-products. The resulting wet mass, generally
containing 40 to 60 percent moisture, is referred to in the art by several names, including hydrolyzed **cellulose**, microcrystalline **cellulose**, microcrystalline **cellulose** wetcake, or simply wetcake. This microcrystalline **cellulose** wetcake may be used as such or may be further modified, for example, by attrition and/or drying, and utilized in.

SUMM Microcrystalline **cellulose** may also be produced for use in the present invention using a steam explosion treatment. In this process, wood
chips
or other **cellulosic** materials are placed in a chamber into which super-heated steam is introduced. After being maintained for a period
of
about 1-5 minutes, the exit valve is opened rapidly, **releasing** the contents explosively and yielding microcrystalline **cellulose**. No additional acid need be introduced into the reaction mixture, since it is believed that the acidic materials in the wood chips and the elevated
temperature and pressure hydrolyze the **cellulose** and degrade it. In addition to the specific forms of microcrystalline **cellulose**, the present invention also contemplates the use of microcrystalline derivatives, including microcrystalized **cellulose**, also known as microcrystallized microcrystalline **cellulose**, and powdered **cellulose**

L57 ANSWER 31 OF 79 USPATFULL on STN (Continued)
such as a commercial material sold as "Solka Floc®."
SUMM As discussed in greater detail below, the microcrystalline **cellulose** preferred for use in the present invention is microcrystalline **cellulose** which has an average particle size below about 100 microns, preferably microcrystalline **cellulose** which been attrited or has an average particle size in the range of 1 to 50 microns, preferably 1 to.

SUMM Carrageenan is used in combination with microcrystaline **cellulose** to form the elegant prompt **release coatings** of the present invention. **Carrageenan** for use in the present invention is a naturally derived carrageenan, including the grades further defined below as iota,
kappa,. . . sulfate content of iota carrageenan may range from about 25% to 34%, preferably about 32%. The iota carrageenan which is **carrageenan** which has a **25%** ester sulfate content and lambda carrageenan which has a 37% ester sulfate content. The calcium salt of iota carrageenan is . . . iota carrageenan require heating water to different temperatures to dissolve them. The iota carrageenan which are
suitable for the microcrystalline **cellulose**/iota carrageenan material of this invention are soluble in water heated up to 60° C. (176° F.). Preferred grades of iota . . .

SUMM The microcrystalline **cellulose** and carrageenan may be coprocessed or may be blended in any suitable manner, such as dry blending. Coprocessed microcrystalline **cellulose**/iota carrageenan is rapidly peptizable. Peptization means that the dry material can readily be dispersed in water in a colloidal state. . . . be dispersed
[peptized]
in a colloidal state with minimal agitation. Thus, the novel coating formulations in which the coprocessed microcrystalline **cellulose**/iota carrageenan is incorporated can be hydrated in as little as 0.5 hour, but more preferably requires 1 to 2 hours.

SUMM The coprocessed microcrystalline/iota carrageenan compositions useful in
this invention may be prepared by first attriting hydrolyzed **cellulose** wetcake, such that the average size of the wetcake particles is at which
generally not more than about 20 microns, preferably . . . at which the particular grade of iota carrageenan being used dissolves, adding the dry carrageenan to the dispersion of microcrystalline **cellulose**, mixing the components, preferably homogenizing the mixture to ensure intimate mixing, and drying the slurry to powder. Spray-drying is used to. . . .

SUMM It is possible to prepare the coatings directly, that is, before the drying of the wetcake, from a dispersion of microcrystalline **cellulose** wetcake and the carrageenan by screening for the water present in the wetcake and adding the other ingredients as the. . . . costs for a dispersion would be less economical. Furthermore, drying by any method may enhance the association of the microcrystalline **cellulose** with the carrageenan, which may not provide satisfactory prompt **release** coating.

SUMM Dry blended microcrystalline **cellulose** (e.g., Avicel® PH-105, average particle size 20 microns) and iota **carrageenan**, has been found to provide **coating** compositions that are at least equal to, and

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in some cases, superior to, coating compositions prepared from coprocessed microcrystalline **cellulose**/carrageenan.
. . . thereof is spread on a surface and allowed to dry. However, the
film is considered to be too weak for **pharmaceutical** tablets as shown by the results in Comparative Example A and therefore requires the presence of microcrystalline **cellulose** for satisfactory results.

SUMM A dry, physical blend of iota carrageenan and microcrystalline **cellulose** (Avicel® PH-105, particle size 20 microns) also yielded what appear to be commercially unsatisfactory results in Comparative Example B. For commercial purposes, it is believed that the average particle size of the microcrystalline **cellulose** used in a dry blend with the naturally occurring hydrocolloid should be below 100 microns, advantageously below about 50. . . . high performance coating formulations. It is the scope of this invention may be prepared from such dry, physical blends of microcrystalline **cellulose** and carrageenan.

SUMM The weight ratio of microcrystalline **cellulose** to carrageenan in the compositions of this invention will depending on the application, but generally range from about 90:10. . . . different ratios of coprocessed material. Thus, the dry, physical blends provide significantly greater flexibility for specific applications having different requirements. Coprocessed veterinary solid dosage forms containing certain active ingredients may require increased carrageenan content in the composition to ideally coat the tablet. For these **pharmaceutical** and veterinary applications, a preferred weight ratio of microcrystalline **cellulose** to carrageenan is in the range of about 75:25 to about 65:35.

SUMM Regardless of whether the composition is based on coprocessed microcrystalline **cellulose**/carrageenan or a dry, physical blend of microcrystalline **cellulose** and carrageenan, a secondary polymer, preferably, **hydroxyethylcellulose**, a plasticizer or both a strengthening polymer and a plasticizer are present in the coating formulation of this invention. While.

SUMM This strengthening polymer which can provide the same benefit and may be used instead of HEC include HPMC, **hydroxypropylcellulose**, **ethylcellulose**, **methylcellulose** and **polyvinylpyrrolidone** (PVP); however, care must be exercised in the selection of any of these
materials
to avoid significantly retarding **release** of active ingredients and/or bioavailability. The preferred amount of strengthening polymer is less than the total amount of microcrystalline **cellulose** and carrageenan present in the composition. Depending on the desired hardness of the coating, the strengthening polymer may be employed . . . polymer is irrelevant to the formulation. Strengthening polymers suitable for use in this invention and which significantly retard **release** from tablets or other solid dosage forms, are those polymers having a viscosity equal to or less than 20 mPa.multidot.s . . .

SUMM . . . following optional ingredients are also contemplated and within
the scope of the coating compositions of the present invention. The prompt **release** coating compositions of the invention may include at least one filler. Such fillers may include, for example, calcium carbonate, dicalcium . . . carbohydrates, such as starch, maltodextrin, lactose, mannitol and other sugars. Of these, maltodextrin
and mannitol are preferred fillers. The prompt **release** coating compositions of the invention may include at least one surfactant. Such

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surfactants include either anionic or nonionic surfactants. Useful. .

SUMM . . . basis a preferred composition of this invention comprises at least about 43%, suitably about 45% to about 75% of microcrystalline **cellulose** and carrageenan powder combined, more preferably about 45% to about 60%; about 0.5% to about 30% of strengthening polymer, more.

SUMM . . . may be preferable to maintain agitation of the aqueous dispersion during the entire period of its being sprayed onto the **pharmaceutical** or veterinary solid dosage forms, confectionary seeds, animal feed, fertilizer, pesticide tablets, or food.

SUMM The preferred edible, hardenable, film-forming coating formulations of this invention may generally be prepared and used according to a simple procedure. A dry blend of coprocessed microcrystalline **cellulose**/carrageenan powder or a dry blend of microcrystalline **cellulose** and carrageenan, and a strengthening polymer such as **hydroxypropylcellulose**, polyethylene glycol or other acceptable plasticizer, optionally together with a solid filler such as maltodextrin, lactose, mannitol or the like.

SUMM In the formulations of microcrystalline **cellulose** and iota carrageenan, a simple propeller mixer provides adequate agitation for rapid hydration. The viscosity and thixotropic or thixotrogic behavior of a formulation which sets up during overnight storage.

Unlike
coating formulations based primarily on hydroxyalkyl ethers of **cellulose**, for example, HPMC, agitation during . . . the microcrystalline and carrageenan-based formulations of this invention does not need to be continued for
. . . Engineering. Equipment variables which one skilled in the art can manipulate to provide an elegant coating based on the microcrystalline **cellulose** and carrageenan materials, either coprocessed or dry blended, include inlet temperature, outlet temperature, air flow, speed of rotation of the.

SUMM **Hydroxypropylcellulose** dissolves more effectively than carrageenan does. Thus, the presence of the major amount of carrageenan in the formulations of . . . the carrageenan which dilutes the negative effect of HEC on drying time. This effect of low melting sensitive **pharmaceutical** agents, for example, ibuprofen, the outlet temperature can be reduced and still provide short enough drying time to be commercially.

SUMM **Hydroxypropylcellulose** is particularly susceptible to clogging spray nozzles at high temperatures. An additional benefit provided by the formulations of this invention.

SUMM The level of coating applied to **pharmaceutical** or veterinary dosage forms is preferably between about 1.5% to about 4% by weight of the uncoated dosage form, more.

SUMM . . . to those of the uncoated tablets used as a substrate for coating. This is an additional unexpected benefit of the coatings based on **carrageenan** and microcrystalline **cellulose**, and it differs from the known drawbacks of HPMC.

SUMM All components of the formulation are typically **pharmaceutically** acceptable, edible food grade materials.

DETD In a Patterson-Kelley twin shell blender were placed 14.43 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), **18.**36 grams of **polyvinylpyrrolidone** (PVP) (GAF), 18.40 grams of polyethylene glycol 8000 (Union Carbide Corporation), and 0.2 gram of yellow #5 food color. After

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DETD By the method of Example 1 a dry mixture of 18.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/Iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 4400, Hercules Incorporated), 10.40 grams of polyethylene glycol 8000, and 0.30 gram of
yellow #5 food color was added. . .
DETD By the method of Example 1, a dry mixture of 19.05 grams of spray-dried,
coprocessed microcrystalline **cellulose**/Iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250 L, Hercules Incorporated), 5.40 grams of polyethylene glycol 8000, 5.0 grams of Micro-Talc, and 0.30 gram of
yellow #5 food color was added.
DETD By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/Iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250L, Hercules Incorporated), 10.40 grams of polyethylene glycol 8000, and 0.30 gram of
yellow #5 food color was added.
DETD By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/Iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250L, Hercules Incorporated), 10.40 grams of polyethylene glycol 8000, 0.30 gram of yellow #5 food color, and 0.10 gram. . . resulting viscous solution was sprayed using a Vector High Coater LDCS onto 1 Kg of cores comprised
of 20% microcrystalline **cellulose** and 80% calcium carbonate, each weighing on average 1.05 grams. Conditions used include an inlet temperature of 77-80° C., and
DETD By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/Iota **carrageenan** (70:30), 10.65 grams of polyethylene glycol 8000, and 0.30 gram of yellow #5 food color was added to 60 grams of deionized. . . stirred while it was sprayed using a Vector High Coater LDCS onto 1 Kg of the same cores of microcrystalline **cellulose** and calcium carbonate that were coated in Example 5. Conditions used include an inlet temperature of 78-79° C., an outlet. . . and a wt. % of 37° C. was less than 3 hours. This coating was not as elegant as coatings containing **hydroxyethylcellulose**.
DETD By the method of Example 3 a dry mixture of 20.95 grams of spray-dried, coprocessed microcrystalline **cellulose**/Iota **carrageenan** (70:30), 2.55 gram of **hydroxyethylcellulose** 250 L, 11.40 grams of polyethylene glycol 8000, and 0.10 gram of yellow #5 food color was added to 450 grams. . . solution was continously stirred while it was sprayed using a Vector High Coater LDCS onto 1.03 Kg of coexpressed microcrystalline **cellulose** cores (Avicel® PH-200) debossed with an FMC logo, each weighing on average 0.267 gram. Conditions used include an inlet temperature.
DETD By the method of Example 1 a dry mixture of 285.75 grams of spray-dried,
coprocessed microcrystalline **cellulose**/Iota **carrageenan** (90:10), 7.5 grams of **hydroxyethylcellulose** 250 L, 156.0 grams of polyethylene glycol 8000, and 45.0 grams of hydrophilic red iron oxide was prepared. A portion. . . have as elegant an appearance as those prepared in Examples 1 through 7 in which the 70:30 combination of microcrystalline

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cellulose and iota carrageenan was employed. Friability testing was satisfactory, but there was minor chipping and erosion observed for these coated.
DETD By the method of Example 1 a dry mixture of 190.8 grams of spray-dried, coprocessed microcrystalline **cellulose**/Iota carrageenan (70:30), 5.02 grams of **hydroxyethylcellulose** 250 L, 104.2 grams of polyethylene glycol 8000, 1.5 grams of methyl paraben, 0.15 gram of propyl paraben, 18.40 grams
DETD By the method of Example 1 a dry mixture of 194.7 grams of spray-dried, coprocessed microcrystalline **cellulose**/Iota carrageenan (70:30), 5.11 grams of **hydroxyethylcellulose** 250 L, 106.4 grams of polyethylene glycol 8000, 1.65 grams of methyl paraben, 0.165 gram of propyl paraben,
18.48 grams.
DETD By the method of Example 1 a dry mixture of 68.94 grams of spray-dried, coprocessed microcrystalline **cellulose**/Iota **carrageenan** (70:30), 1.81 grams of **hydroxyethylcellulose** 250 L, 37.67 grams of polyethylene glycol 8000, 0.545 grams of methyl paraben, 0.0545 gram of propyl paraben, 10.24 grams.
DETD In a Patterson-Kelley twin shell blender were placed 229.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 160.65 grams) and iota carrageenan (68.85 grams), 49.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 148.5 grams of polyethylene glycol 8000 (Union Carbide Corporation), 13.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation),
DETD By the method of Example 12, a dry blend comprising 238.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 166.95 grams) and iota carrageenan (71.55 grams), 40.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 148.5 grams of polyethylene glycol 8000 (Union Carbide Corporation), 13.5 grams of maltodextrin (Maltrin M-180), and 9.0 grams. . . at 50 rpm, 900 ml 0.05 M phosphate buffer at 35 minutes showed that 100% of the acetaminophen had been **released** at pH 5.8 and 97% at the ibuprofen had been **released** at pH 7.2. Dissolution testing using apparatus 1 (basket) at 50 rpm, 500 ml 0.05 M acetate buffer, pH 4.5 showed that 93% of the caplets had been **released**.
DETD By the method of Example 12, a dry blend comprising 238.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 166.95 grams) and iota carrageenan (71.55 grams), 40.5 grams of **hydroxyethylcellulose** (Aqualon® 250 L), 148.5 grams of polyethylene glycol 8000 (Union Carbide Corporation), and 22.5 grams of maltodextrin (Maltrin M-180), was. . . 90° C. Hydration required 75 minutes. A Acrela-Cota coater was charged with 12 Kg of cores comprised of 20% microcrystalline **cellulose** and 80% calcium carbonate, each weighing on average 1.05 grams. The coater was operated at an inlet temperature of 82.8-100.2°.
DETD In a Patterson-Kelley twin shell blender were placed 234.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 166.5 grams) and iota carrageenan (67.5 grams), 67.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 63.0 grams of maltodextrin (Maltrin® M-100, Grain Processing Corporation), 63.0 grams of titanium dioxide, and 22.5 grams of. . .
DETD In a Patterson-Kelley twin shell blender were placed 76.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams)

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and iota **carrageenan** (21.0 grams), 32.5 grams of **hydroxyethylcellulose** (Aqualon® 250 L), 28.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), 10.0 grams of Red #40 aluminum lake, and.
DETD In a Patterson-Kelley twin shell blender were placed 76.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (21.0 grams), 32.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 28.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), 10.0 grams of a red dye blend (Warner Jenkinson), .
DETD In a larger Patterson-Kelley twin shell blender were placed 1.940 Kg of a
blend of microcrystalline **cellulose** (Avicel® PH-105, 1.358 Kg) and iota carrageenan (0.582 Kg), 0.436 Kg of **hydroxyethylcellulose** (Aqualon® 250L), 0.277 Kg of maltodextrin (Maltrin® M-180, Grain Processing Corporation), and 1.307 Kg of polyethylene glycol 8000 (Union
Carbide.
DETD In a Patterson-Kelley twin shell blender were placed 72.80 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 56 .25 grams) and iota **carrageenan** (18.0 grams), 33.08 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 64.15 grams of hydrophilic red iron oxide. After being thoroughly mixed, the dry components were added to. . .
DETD In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (21.0 grams), 32.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 13.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), and 22.5 grams of hydrophilic yellow oxide. After
DETD In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (18.0 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 21.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation). Simultaneously 22.5 grams of titanium dioxide was added. .
DETD In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**18**.0 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 12.0 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation). Simultaneously 21.5 grams of titanium dioxide was added. .
DETD In a Patterson-Kelley twin shell blender were placed 78.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (22.5 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 3.0 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation). Simultaneously 30.5 grams of titanium dioxide was added. .
DETD In a Patterson-Kelley twin shell blender were placed 71.33 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 49.94 grams) and iota **carrageenan** (21.39 grams), **16**.01 grams of **hydroxyethylcellulose** (Aqualon® 250L), 48.05 grams of polyethylene glycol 8000 (Union Carbide Corporation), 10.19 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation). . .
DETD In a Patterson-Kelley twin shell blender were placed 78.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (22.5 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 1.5 gram of stearic

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acid. Simultaneously 37.5 grams of titanium dioxide was added to 1516.7 grams of.
DETD In a Patterson-Kelley twin shell blender were placed 390 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, **200** grams) and iota **carrageenan** (**100** grams), and **100** grams of polethylene glycol 8000 (Union Carbide Corporation). After the dry components had been thoroughly blended, the entire blend was.
DETD In a Patterson-Kelley twin shell blender were placed 49.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 34.3 grams) and iota **carrageenan** (**14**.7 grams), **11**.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), 33.0 grams of polyethylene glycol 8000 (Union Carbide Corporation), 7.0 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation),
DETD In a Patterson-Kelley twin shell blender were placed 43.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 23 grams) and iota **carrageenan** (**10** grams), **20** grams of **hydroxyethylcellulose** (Aqualon® 250L), 25.0 trans of triacetin, 6.0 grams of propylene glycol alginate, and 3 grams of Fluronic F-68 (BASF). After. . .

DETD

Ingredient Amount (g)

Microcrystalline **cellulose** 37.5
(Avicel PH-**105**)
Iota **carrageenan** **14**.7
Polyethylene glycol 8000 34
Hydroxyethylcellulose 250L 11
Maltodextrin M-180 3

DETD

31 32 33
Example: Weight (grams)

Avicel PH-105 28 34.3 34.3
Iota **carrageenan** **11** **14**.7 **14**.7
Hydroxyethylcellulose -- 11 11
PGB.sup.a. 34 34 34
PEG.sup.b 34 33 33
Triacetin.sup.c 5 7.4 7
Maltrin M-180 3 3 3
. . .
.sup.aPropylene glycol. . .

DETD

Weight (grams)

Avicel PH-**105** 33
Iota **carrageenan** **10**
Hydroxyethylcellulose 20
PGB.sup.a 4
Fluronic F-68 3
. . .
.sup.aPropylene glycol alginate (Protonal ® ester SD-LB, Pronova)

DETD

Ingredient Weight (grams)

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Avicel PH-105 37
Iota **carrageenan** 14.5
Hydroxyethylcellulose 22
Mannitol,sup.a 15.5
Pluronic F-68 3
Blue Lake #2 8
Deionized water 1150
Hydration time 2.5
Caplets
Impingofen 1 kg
Avetamingfen.
DETD A dispersion of 9.30 grams of microcrystalline **cellulose** (Avicel® PH-102, FMC Corporation) and 20.7 grams of iota carrageenan (Viscarin® SD-389) in 1700 grams of deionized water was prepared.

CLM What is claimed is:
1. An edible, hardenable, prompt **release**, **pharmaceutical** and veterinary coating composition comprising a dry blend of (a) microcrystalline **cellulose** having an average particle size less than 100 microns, (b) a film forming amount of carrageenan, and (c) at least one of a strengthening polymer and a plasticizer, wherein the weight ratio of microcrystalline **cellulose** to carrageenan is in the range of about 90:10 to about 60:40 wherein said coating composition does not, when ingested or placed in an aqueous medium, significantly retard **release** of active ingredients from a **pharmaceutical** and veterinary solid dosage form to which said coating is applied.

CLM What is claimed is:
2. The coating composition of claim **1**, wherein the **carrageenan** is iota carrageenan.

CLM What is claimed is:
4. The coating composition of claim 3, wherein said strengthening polymer is selected from the group consisting of **hydroxyethylcellulose**, **hydroxypropylmethylcellulose**, **hydroxypropylcellulose**, **ethylcellulose**, **methylcellulose**, and **polyvinylpyrrolidone**.

CLM What is claimed is:
5. The coating composition of claim 3, wherein the strengthening polymer is **hydroxyethylcellulose**.

CLM What is claimed is:
16. The coating composition of claim 1, wherein the microcrystalline **cellulose** has an average particle size in the range of 1 to 50 microns.

CLM What is claimed is:
17. The coating composition of claim 16, wherein the microcrystalline **cellulose** has an average particle size in the range of about 1 to about 30 microns.

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CLM What is claimed is:
28. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, high molecular weight polyethylene glycol and a coloring agent, wherein said microcrystalline **cellulose** has a particle size less than 50 microns wherein the weight ratio of microcrystalline **cellulose** to iota carrageenan is in the range of about 90:10 to about 60:40.

CLM What is claimed is:
29. A dry **coating** composition comprising microcrystalline **cellulose**, **carrageenan** and at least one of a strengthening polymer and a plasticizer, wherein said dry composition can be hydrated in a period of 0.3-3 hours at ambient temperature wherein the weight ratio of microcrystalline **cellulose** to iota carrageenan is in the range of about 90:10 to about 60:40.

CLM What is claimed is:
31. A method for coating a **pharmaceutical** or veterinary solid dosage form comprising the steps of hydrating the dry blended coating composition wherein the coating composition comprises a dry blend of (a) microcrystalline **cellulose** having an average particle size less than 100 microns, (b) a film forming amount of carrageenan, and (c) at least one polymer and a plasticizer, wherein said coating composition does not, when ingested or placed in a aqueous medium, significantly retard **release** of active ingredients from a **pharmaceutical** and veterinary solid dosage form to which said coating is applied, followed by spray coating said hydrated coating composition onto said **pharmaceutical** or veterinary solid dosage form.

CLM What is claimed is:
32. An edible, hardenable, prompt **release** **pharmaceutical** and veterinary coating composition comprising a dry blend of (a) microcrystalline **cellulose**, (b) a film forming amount of carrageenan, and (c) at least one of a strengthening polymer and a plasticizer, wherein the weight ratio of microcrystalline **cellulose** to carrageenan is in the range of about 90:10 to about 60:40, wherein said coating composition does not, when ingested or placed in an aqueous medium significantly retard **release** of active ingredients from a **pharmaceutical** and veterinary solid dosage form to which said coating is applied.

CLM What is claimed is:
34. A **pharmaceutical** and veterinary tablet coated with the coating composition of claim 32.

CLM What is claimed is:
35. A **pharmaceutical** and veterinary tablet coated with the coating composition of claim 1.

CLM What is claimed is:
36. A dry edible, hardenable, prompt **release**, **pharmaceutical** and veterinary coating composition comprising (a) microcrystalline **cellulose**, (b) a film forming amount of carrageenan, and (c) at least one of a strengthening polymer and a plasticizer, wherein the weight ratio of microcrystalline **cellulose** to carrageenan is in the range of

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CLM What is claimed is:
19. A **pharmaceutical** or veterinary solid dosage form coated with an edible, hardenable, prompt **release** coating composition wherein the coating composition comprises a dry blend of (a) microcrystalline **cellulose** having an average particle size less than 100 microns, (b) a film forming amount of carrageenan, and (c) at least one polymer and a plasticizer, wherein said coating composition does not, when ingested or placed in an aqueous medium, significantly retard **release** of active ingredients from a **pharmaceutical** and veterinary solid dosage form to which said coating is applied.

CLM What is claimed is:
20. The **pharmaceutical** or veterinary solid dosage form of claim 19, wherein the coating is applied to the solid dosage form at a level.

CLM What is claimed is:
21. The **pharmaceutical** or veterinary solid dosage form of claim 20, wherein the coating is applied to the dosage form at a level.

CLM What is claimed is:
22. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, high molecular weight polyethylene glycol and maltodextrin, wherein said microcrystalline **cellulose** has a particle size less than 50 microns wherein the weight ratio of microcrystalline **cellulose** to iota carrageenan is in the range of about 90:10 to about 60:40.

CLM What is claimed is:
23. A **pharmaceutical** solid dosage form comprising the edible coating composition of claim 22.

CLM What is claimed is:
24. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, mannitol, a surfactant and a coloring agent, wherein said microcrystalline **cellulose** has a particle size less than 50 microns wherein the weight ratio of microcrystalline **cellulose** to iota carrageenan is in the range of about 90:10 to about 60:40.

CLM What is claimed is:
25. A **pharmaceutical** solid dosage form comprising the edible coating composition of claim 24.

CLM What is claimed is:
26. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, and a coloring agent, wherein said microcrystalline **cellulose** has a particle size less than 50 microns wherein the weight ratio of microcrystalline **cellulose** to iota carrageenan is in the range of about 90:10 to about 60:40.

CLM What is claimed is:
27. A **pharmaceutical** solid dosage form comprising the edible coating composition of claim 26.

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ACCESSION NUMBER: 2002:196319 USPATFULL
TITLE: Oral **pharmaceutical** preparation comprising an antiulcer activity compound, and process for its production
INVENTOR(S): Sarder, Carlos Picorrell, Madrid, SPAIN

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002209562	A1	20020725	
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DOCUMENT TYPE:	Utility		
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LEGAL REPRESENTATIVE:	THOMAS C. FONTAINE, ESQ., COZEN O'CONNOR 1133 Avenue of the Americas		
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EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	0 Drawing Page(s)		
LINE COUNT:	941		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed is a **pharmaceutical** preparation and a process for making the same. The preparation has an inert nucleus; an active layer which is soluble or disintegrates rapidly in water, obtained from a single aqueous or hydroalcoholic solution-suspension which includes: an active ingredient of anti-ulcerous activity of formula I, II or III, and at least one excipient; and a gastro-resistant outer coating layer obtained from a solution which includes an enteric coating polymer and at least one excipient. The process is conducted by coating the inert nucleu by spraying a single aqueous or hydroalcoholic suspension-solution onto the nucleu; drying of the active layer formed during the spraying; and coating the charged nuclei by spraying of a solution which includes an enteric coating polymer with at least one excipient in order to obtain a gastro-resistant outer coating layer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Oral **pharmaceutical** preparation comprising an antiulcer activity compound, and process for its production

AB Disclosed is a **pharmaceutical** preparation and a process for making the same. The preparation has an inert nucleus; an active layer which is soluble. . .

SUMM [0002] The present invention relates to a new **pharmaceutical** formulation for oral administration which includes a compound of anti-ulcer activity, and to a procedure for making same.

L57 ANSWER 32 OF 79 USPATFULL on STN (Continued)
polyoxyethylene glycol, castor oil, **cellulose** phthalic acetate, phthalate of HPMC, succinate acetate of HPC, sodium carboxymethylamylopectin, chitosan, alginic acid, **carrageenans**, galactomannans, tragacanth, **wheilac**, agar-agar, gum arabic, guar gun and xanthan gum, polyacrylic acids, methacrylics and their salts, HPMC acetate succinate, **polyvinyl** acetate phthalate, **cellulose** acetate trimethylate, **polyvinyl** alcohol (PVA), polyethylene and polypropylene oxides and mixtures thereof. The gastro-resistant polymer can be accompanied by: plasticizers such as triethylcitrate. . . .

DETD [0064] The procedure for obtaining the oral **pharmaceutical** preparation of the invention is as follows:

DETD [0067] at least one **pharmaceutically** acceptable excipient selected from the group which includes: a binder, an alkaline reaction compound, a surface-active agent, a filling material.

DETD . . . 1) coating of the nuclei by spraying a solution which contains an enteric coating polymer with at least one **pharmaceutically** acceptable excipient selected from the group which includes: a plasticizer, a surface-active agent, a pigment and a lubricant, in order . . .

DETD . . . lactose and sodium lauryl sulphate, with continuous agitation throughout. When the mixture was homogeneous the colloidal aqueous solution of hydroxypropylmethyl **cellulose** (13.50% p/p) was added, maintaining agitation in order to ensure homogeneity of the product. L-HPC was then incorporated into that. . . . the neutral pellets.

Lansoprazol	1.29	Kg
Sodium lauryl sulphate	5.28 10.sup.-3	Kg
Chrystallized disodium phosphate	0.052	Kg
Hydroxypropylmethyl **cellulose**	0.8	Kg
Lactose	0.51	Kg
Hydroxypropyl **cellulose**	0.39	Kg
Water	14.28	Kg

DETD . . . pellets under different storage conditions: ambient temperature, and 40° C. and relative humidity 75%.

Test	Gastro-Transmittance Colour	resistence **Release**	Active Ing.	Humidity	at
	440 nm				

Storage conditions: Ambient temperature
Container: Topaz glass bottle with bag of silica gel inside fitted with metallic . . .

DETD [0068] No significant differences were found in the values for gastro-resistance and **release** of active ingredient with respect to the initial values, independently of the storage conditions. Both tests were carried out according to **Pharmacopea** USP XXIII.

DETD . . . added the omeprazol, lactose and sodium lauryl sulphate. Agitation was maintained to total homogeneity and the colloidal solution of hydroxypropylmethyl **cellulose** (12.55% p/p) and hydroxypropyl **cellulose** (L-HPC) added. Agitation was maintained up till the moment of spraying onto the neutral pellets.

DETD . . . was as follows:

L57 ANSWER 32 OF 79 USPATFULL on STN (Continued)

Omeprazol	1.38	Kg
Sodium lauryl sulphate	5.28 10.sup.-3	Kg
Chrystallized disodium phosphate	0.052	Kg
Hydroxypropylmethyl **cellulose**	0.68	Kg
Lactose	0.51	Kg
Hydroxypropyl **cellulose**	0.39	Kg
Water	14.28	Kg

DETD glycol 6000 0.18 Kg
Polycarbate 0.08 Kg
Eudragik L30D55 5.76 Kg
Water 12.14 Kg
Formula II
Acetone 20.84 Kg
Hydroxypropylmethyl **cellulose** phthalate 2.35 Kg
Diethyl phthalate 0.211 Kg
Etyl alcohol 8.93 Kg

DETD . . . Omeprazol under different storage conditions: ambient temperature, and 30° C. and relative humidity 65%.

Test	Gastro-Transmittance Colour	resistence **Release**	Active Ing.	Humidity	at
	440 nm				

Storage conditions: Ambient temperature
Container: Topaz glass bottle with bag of silica gel inside fitted with metallic . . .
DETD [0102] The gastro-resistance, humidity and and **release** values explain the physical stability of the pellet under the storage conditions tested. For their part, the power of the.
DETD [0105]

Omeprazol	1.51	Kg
Sodium lauryl sulphate	5.28 10.sup.-2	Kg
Hydroxypropylmethyl **cellulose**	1.09	Kg
Lactose	1.35	Kg
Hydroxypropyl **cellulose**	0.54	Kg
Sodium acetate	7.20 10.sup.-2	Kg
Water	17.64	Kg

DETD . . . . . The dry granules were then subjected to enteric coating by spraying any of the gastro-resistant solution-suspension detailed below.

Hydroxypropylmethylcellulose	1.617	Kg
acetate succunate (AS-MF)		
Triethylcitrate	0.45	Kg
Talc	0.48	Kg g
Sorbitan sesquioleate	4.04 10.sup.-4	Kg
Water	13.62	Kg.

CLM What is claimed is:
1. An oral **pharmaceutical** preparation comprising: a) an inert nucleus; b) a soluble active layer or layer which disintegrates rapidly

L57 ANSWER 32 OF 79 USPATFULL on STN (Continued)
in water, made from . . . n is a whole number from 0 to 4; or of formula II or III, ##STR3## and at least one **pharmaceutically** acceptable excipient selected from the group which includes: a binder, an alkaline reaction compound, a surface-active agent, a filling material. . .
CLM What is claimed is:
2. The **pharmaceutical** preparation of claim 1, wherein the inert nucleus is a neutral spherical microgranule which includes an its composition at least two of: sorbical, mannitol, saccharose, starch, microcrystalline **cellulose**, lactose, glucose, trehalose, maltitol or fructose.

CLM What is claimed is:
3. The **pharmaceutical** preparation of claim 1, wherein the inert nucleus has an imitial size between 200 and 1900 micrometers, preferably between 600-900. . .
CLM What is claimed is:
4. The **pharmaceutical** preparation of claim 1, wherein the binder in said agenera or hydroalcoholic solution-suspension is selected from the group consisting of saccharose, starch, methyl **cellulose**, CMC, HPC, HPMC, **polyvinyl** pyrrolidone (PVP), dextrin or gum arabic, dissolved in water, ethanol, or a mixture of both at 50% (v/v).

CLM What is claimed is:
5. The **pharmaceutical** preparation of claim 1, wherein the compound of alkaline reaction in said aqueous or hydroalcoholic solution-suspension is selected from the. . .
CLM What is claimed is:
6. The **pharmaceutical** preparation of claim 1, wherein the surface-active agent in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting. . .
CLM What is claimed is:
7. The **pharmaceutical** preparation of claim 1, wherein said filling material in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of lactose, starch, saccharose and microcrystalline **cellulose**.

CLM What is claimed is:
8. The **pharmaceutical** preparation of claim 1, wherein said disintegrating-swelling excipient in said aqueous or hydroalcoholic solution suspension is selected from the group. . .
CLM What is claimed is:
9. The **pharmaceutical** preparation of claim 1, wherein said enteric coating polymer in said external gastro-resistant coating is selected from the group consisting of methyl **cellulose**, HEC, HPC, HPMC, ethyl **cellulose**, HEC, HPC, polyoxyethylene glycol, castor oil, **cellulose** phthalic acetate, phthalate of HPMC, succinate acetate of HMC, sodium carboxymethylamylopectin, chitosan, alginic acid, **carrageenans**, galactomannans, tragacanth, **xhellac**, agar-agar, gum arabic, guar gun, xanthan gum, polyacrylic acids, methacrylics and their salts, PVA, polyethylene and polypropylene oxides and mixtures.
CLM What is claimed is:
10. The **pharmaceutical** preparation of claim 1, wherein said

L57 ANSWER 32 OF 79 USPATFULL on STN (Continued)
plasticizer in said external gastro-resistant coating is selected from the group consisting of TEC, . . .
CLM What is claimed is:
11. The **pharmaceutical** preparation of claim 1, wherein said surface-active agent present in said external gastro-resistant coating layer is selected from the group. . .
CLM What is claimed is:
12. The **pharmaceutical** preparation of claim 1, wherein said pigment in said external gastro-resistant coating layer is selected from the group consisting of. . .
CLM What is claimed is:
13. The **pharmaceutical** preparation of claim 1, wherein said lubricant in said external gastro-resistant coating layer is selected from the group consisting of. . .
CLM What is claimed is:
14. A process for making an oral **pharmaceutical** preparation comprising: a) coating inert nuclei to form a layer thereon by spraying
aqueous or hydroalcoholic suspension-solution, which comprises: an. . . n is a whole number from 0 to 4; or general formula II or III, ##STR3## and at least one **pharmaceutically** acceptable excipient selected from the group which includes: a binder, an alkaline reaction compound, surface-active agents, a filling material and. . . and c) coating the charged nuclei by spraying a solution which contains an enteric coating polymer with at least one **pharmaceutically** acceptable excipient selected from the group comprising: a plasticizer, a surface-active agent, a pigment and a lubricant, to form an. . .
CLM What is claimed is:
. . . claim 14, wherein said binder in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of saccharose, starch, **methylcellulose**, CMC, HPC, HPMC, **polyvinyl** pyrrolidone (PVP), dextrin or gum arabic, either alone or mixed, dissolved in water, ethanol or a mixture of both at. . .
CLM What is claimed is:
. . . filling material in said aqueous or hydroalcoholic solution-suspension is selected from the group consisting of lactose, starch, saccharose and microcrystalline **cellulose**.

CLM What is claimed is:
. . . claim 14, wherein said enteric coating polymer in said external gastro-resistant coating is selected from the group consisting of methyl
cellulose, HEC, HPC, HPMC, ethyl **cellulose**, HEC, HPC, polyoxyethylene glycol, castor oil, **cellulose** phthalic acetate, phthalate of HPMC, succinate acetate of HMC, sodium carboxymethylamylopectin, chitosan, alginic acid, **carrageenans**, galactomannans, tragacanth, **xhellac**, agar-agar, gum arabic, guar gun, xanthan gum, polyacrylic acids, methacrylics and their salts, PVA, polyethylene and polypropylene oxides and mixtures. . . .
CLM What is claimed is:
26. The **pharmaceutical** preparation of claim 1 wherein the filling material is selected from the group consisting of mannitol, sorbitol or

L57 ANSWER 33 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2002:160556 USPATFULL
TITLE: Granule containing protein and corn starch layered on an inert particle
INVENTOR(S): Becker, Nathaniel T., Hillsborough, CA, United States
Green, Thomas S., Novrato, CA, United States
PATENT ASSIGNEE(S): Genencor International, Inc., Rochester, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6413749	B1	20020702
APPLICATION INFO.:	US 1999-428153		19991027 (9) <--

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-105874P	19981027 (60) <--
DOCUMENT TYPE:	US Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Naff, David M.	
LEGAL REPRESENTATIVE:	Castaneda, Janet Kaiser	
NUMBER OF CLAIMS:	17	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	522	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Granules are prepared containing an admixture of protein and starch layered over an inert particle. Proteins include **pharmaceutically** important proteins such as hormones, or industrially important proteins such as enzymes including proteases, amylases, lipases and cellulases capable of hydrolysing substrates such as stains. Inert particles include inorganic salts, sugars, sugar alcohols, small organic molecules
such as organic acids or salts, and minerals such as clays or silicates.
The admixture may also contain sugar such as sucrose. A ratio of corn starch to sugar much greater than 1:1 such as in a range of about 5:1 to
about 15:1 is preferred. A coating layer may be between the inert particle and the admixture and/or over the admixture. Methods that may be used in preparing the granules include pan-coating, fluid-bed coating, prilling, disc granulation, spray drying, extrusion, centrifugal extrusion, spheronization, drum granulation and high shear agglomeration.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Granules are prepared containing an admixture of protein and starch layered over an inert particle. Proteins include **pharmaceutically** important proteins such as hormones, or industrially important proteins such as enzymes including proteases, amylases, lipases and cellulases capable of. . .
SUMM Proteins such as **pharmaceutically** important proteins like hormones and industrially important proteins like enzymes are becoming more widely used. Enzymes are used in several. . .
SUMM U.S. Pat. No. 4,106,991 describes an improved formulation of enzyme granules by including within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-40% w/w based on the

L57 ANSWER 33 OF 79 USPATFULL on STN (Continued)
dry weight of the whole composition. In addition, this patent. . .
SUMM . . . diatomaceous earth or sodium nitrate crystals. The fin forming
material may be a fatty acid ester, an alkoxylated alcohol, a
SUMM **polyvinyl** alcohol or an ethoxylated alkylphenol.
. . . perborate or sodium percarbonate. Acrowexplaining all these
desired characteristics simultaneously is a particularly challenging
task since, for example, may delayed **release** or low-dust agents such
as fibrous **cellulose** or kaolin leave behind insoluble residues.
. . . between the seed particle and the matrix or the matrix and the
barrier layer, for example, a coating such as **polyvinyl** alcohol (PVA).
SUMM Proteins that are within the scope of the present invention include
pharmaceutically important proteins such as hormones or other
therapeutic proteins and industrially important proteins such as
enzymes.
SUMM . . . more synthetic polymers or other excipients as known to those
skilled in the art. Suitable synthetic polymers include polyethylene
oxide, **polyvinyl** alcohol, **polyvinyl** pyrrolidone, polyethylene glycol
and polyethylene oxide/polypropylene oxide.
SUMM Suitable coatings include water soluble or water dispersible
film-forming polymers such as **polyvinyl** alcohol (PVA); **polyvinyl**
pyrrolidone (PVP); **cellulose** derivatives such as **methylcellulose**,
hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**,
carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene
glycol, polyethylene oxide, gum arabic, xanthan, **carrageenan**,
chitosan, latex polymers, and enteric **coatings**. Furthermore, coating
agents may be used in conjunction with other active agents of the same
or different categories.
SUMM . . . Preferably, the outer coating layer comprises partially
hydrolyzed PVA having low viscosity. Other vinyl polymers which may be
useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful
copolymers include, for example, PVA-methylmethacrylate copolymer and
PVP--PVA copolymer.
DETD . . . monastrally coated with 92.4 kg of an aqueous solution
containing 7.1 kg (6.2% w/w) titanium dioxide, 2.9 kg (2.5% w/w)
methylcellulose, 2.9 kg (2.5%) Pureone 8790, 1.2kg (1.5% w/w) Neodol
23/6.5, and 2.0 kg (1.6% w/w) of polyethylene glycol at a. . .
CLM What is claimed is:
4. The granule of claim 3, wherein the coating is selected from the
group consisting of **polyvinyl** alcohol, **polyvinyl** pyrrolidone,
cellulose derivatives such as **methylcellulose**, hydroxypropyl
methylcellulose, **hydroxycellulose**, **ethylcellulose**, carboxymethyl
cellulose, hydroxypropyl **cellulose**, polyethylene glycol,
polyethylene oxide, chitosan, gum arabic, xanthan and carrageenan.

L57 ANSWER 34 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2002:157579 USPATFULL
TITLE: LOW-DENSITY COMPOSITIONS AND PARTICULATES INCLUDING SAME
INVENTOR(S): CHRISTENSEN, ROBERT I, JR., PIMOLE, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20020082183	A1	20020627
	US 6554466	B2	20030318
APPLICATION INFO.:	US 2000-679691	A1	20000107 (7) <---

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115655P	19990108 (60) <---
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	JEFFREY S FRAZIER, GENNCOE INTERNATIONAL INC, 905 PAGE MILL ROAD, PALO ALTO, CA, 94304	

NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
LINE COUNT: 879
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides low-density compositions, as well as particulates formed, at least in part, from such compositions. Preferred low-density materials include, for example, hollowspheres, low-density minerals, and low-density wood materials (e.g., sawdust). The low-density compositions of the invention can be formed as particulates, or cores, suitable for use in forming enzyme granules, e.g., marums, layered granules, prills, drum granules, agglomerated granules, or the like. Granules are disclosed having advantageous properties, e.g., low dusting, storage stable, fast enzyme-**release** profile, low true density, etc. The granules of the invention are especially useful, for example, in liquid detergents and cleaners, such as predominantly aqueous, liquid laundry detergents. In one embodiment, granules are provided having a true, or volumetric, density within a range of from about 0.95 to about 1.3 g/cm.sup.3. The granules can be economically produced in commercial quantities by way of a marumerization, drum granulation, fluid-bed spray-coating, pan-coating, or other suitable process.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB . . . prills, drum granules, agglomerated granules, or the like. Granules are disclosed having advantageous properties, e.g., low dusting, storage stable, fast enzyme-**release** profile, low true density, etc. The granules of the invention are especially useful, for example, in liquid detergents and cleaners,
SUMM [0003] The use of proteins such as **pharmaceutically** important proteins, e.g., hormones, and industrially important proteins, e.g., enzymes, has been rapidly growing in recent years. Today, for example, .

L57 ANSWER 34 OF 79 USPATFULL on STN (Continued)
a solution containing 7.7% active alkaline protease and 2.1% **polyvinylpyrrolidone** (Luvitabol K-1 7 from BASF) was spray-coated onto the cores. Subsequently, a 40% solution containing 4.8 kg of dry. . . . Kgs of hydrated starch was spray-coated onto the enzyme particulates. Finally, a cosmetic coating solution containing 3.62 Kgs of hydroxypropyl **cellulose** (Methocel 1 from Dow chemical), 4.352 Kgs of titanium dioxide and .731 Kgs of polyethylene glycol (PEG 600) was spray-coated
DETD [0085] e) 600 grams of **cellulose** fibers (Arbocel 600-30)
DETD [0089] g) 39 grams of **polyvinylpyrrolidone** (Luvitabol K-30 from BASF)
DETD . . . of 85.degree. C. fluidizing air. To this, 1710 grams of a 17% w/w total solids solution including 82 grams of hydroxypropyl **cellulose** (Methocel E-15), 99 grams of titanium dioxide and 17 grams of polyethylene glycol (PEG600) was evenorod onto the marums at a
DETD [0096] e) 600 grams of **cellulose** fibers (Arbocel 600-30)
DETD [0100] g) 39 grams of **polyvinylpyrrolidone** (Luvitabol K-30 from BASF)
DETD . . . coated onto the enzyme marum. Subsequently, 1520 grams of a 13% w/w total solids solution including 74 grams of hydroxypropylmethyl **cellulose** (Methocel E-15), 88 grams of titanium dioxide, 20 grams of neodol 23/6.5 (Shell chemical) and 15 grams of polyethylene glycol. .
DETD . . . was spray-coated onto the sucrose seeds. Subsequently, 56.3 Kgs of a 13% w/w total solids solution containing 3.3 Kgs hydroxypropylmethyl **cellulose** (Methocel E-15), 3.3 Kgs titanium dioxide and 0.7 Kgs of polyethylene glycol (PEG 600) was spray coated onto the enzyme.
DETD [0112] Enzyme **release**
DETD [0113] A commonly used method for measuring enzyme **release** from a granule under typical liquid applications conditions is the enzyme dissolution test. In this test, granules are added to. . .
DETD [0114] Granules of the present invention preferably have at least 80%, and preferably at least 90%, of the enzyme activity **released** into the liquor within 5 minutes at 15.degree. C. More preferably, the granules taught herein have a minimum of 90% of the enzyme activity **released** into the liquor within 3 minutes at 15.degree. C. Exemplary granules that have been tested in support of the present invention exhibit an enzyme **release** rate of no less than 90% in 5 minutes at 15.degree. C., and most exhibit an enzyme **release** rate of no less than 90% in 3 minutes at 15.degree. C.

Summary Table

Granule Sample	Volumetric Density (g/ml)
Example. . .	

L57 ANSWER 35 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2002:157138 USPATFULL
TITLE: Coated particles containing an active
INVENTOR(S): Simonsen, Ole, Soborg, DENMARK
Sach, Poul, Birkerod, DENMARK
PATENT ASSIGNEE(S): Novozymes A/S, Bagsvaerd, DENMARK (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002081378	A1	20020627
	US 7070802	B2	20060704
APPLICATION INFO.:	US 2001-964849	A1	20010928 (9) <---

	NUMBER	DATE
PRIORITY INFORMATION:	DK 2000-1466	20001002 <---
	US 2000-239001P	20001006 (60) <---

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: NOVOZYMES NORTH AMERICA, INC., C/O NOVO NORDISK OF NORTH AMERICA, INC., 405 LEXINGTON AVENUE, SUITE 6400, NEW YORK, NY, 10174
NUMBER OF CLAIMS: 37
EXEMPLARY CLAIM: 1
LINE COUNT: 1340
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to coated particles comprising a coating and a core particle comprising an active, wherein the coating comprises a gas phase component. The invention also relates to processes for the manufacture of such coated particles comprising (a) providing a coating material comprising a gas phase component and applying the gas containing coating material to a core particle or (b) providing a coating material comprising a gas generating component, applying the coating material to a core particle and treating the coated particles so as to generate a gas from the gas generating component. Furthermore, it also relates to the use of such coated particles in a number of applications.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM . . . various high-shear mixers can be used as granulators, granulates consisting of the enzyme, fillers and binders etc. are mixed with **cellulose** fibers to reinforce the particles to give the so-called T-granulate. Reinforced particles, being more robust, release less enzyme dust (vide . . .

SUM . . . Also polysaccharides are preferred, such as starch or derivatives thereof. Rudolf® is an example of non-hollow lightweight material made from **cellulose** (non-fibrous from papermaking), available from GranTek Inc. These materials may be included in the granules of the invention either alone . . .

SUM . . . further embodiments wares which are useful in the invention can

L57 ANSWER 35 OF 79 USPATFULL on STN (Continued)
. . . The particle of claim 7, wherein the carbohydrate polymer is selected from the group consisting of pectin, starch, modified starch, **cellulose**, modified **cellulose**, carrageenan, gum Arabic, acacia gum, xanthan gum, locust bean gum and guar gum.

CLM What is claimed is:
. . . The method of claim 23, wherein the carbohydrate polymer is selected from the group consisting of pectin, starch, modified starch, **cellulose**, modified **cellulose**, carageenan, gum Arabic, acacia gum, xanthan gum, locust gum, and guar gum.

CLM What is claimed is:
32. The method of claim 29, wherein the synthetic polymer is selected from the group consisting of **polyvinyl** pyrrolidone (PVP), **polyvinyl** alcohol (PVA), **polyvinyl** acetate, polyacrylate, polymethacrylate, polyarylamide, polyethylene, polyacrylonitrile, and copolymers thereof, preferably water soluble polymers or copolymers.

IT 71-52-3, Bicarbonate, uses 79-10-7D, Acrylic acid, esters, polymers 79-41-4D, Methacrylic acid, esters, polymers 124-38-9, Carbon dioxide, uses 7727-37-9, Nitrogen, uses 9000-01-5, Gum arabic **9000-07-1**, Carrageenan 9000-30-0, Guar gum 9002-60-2, Locust bean gum 9002-69-1, Pectin 9002-90-2, Tragacanth 9002-89-5, Poly(vinyl alcohol) 9003-01-4, Polyacrylamide 9003-20-7, Poly(vinyl acetate) 9003-39-8, PVP 9004-34-6, **Cellulose**, uses 9005-25-8, Starch, uses 9012-76-4, Chitosan 11138-66-2, Xanthan gum 24991-23-9 25322-68-3, Polyethylene glycol 25513-46-6, Poly(glutamic acid) 25608-40-6, Poly(aspartic acid) 26062-13-8, Poly(aspartic acid)
198540-76-5, Expancel 461DE20
(**coated** particles containing active substances for detergent formulations)
IT **9000-07-1**, Carrageenan
(**coated** particles containing active substance for detergent formulations)

L57 ANSWER 36 OF 79 USPATFULL on STN (Continued)
ACCESSION NUMBER: 2002:115839 USPATFULL
TITLE: Rapidly peptizable microcrystalline **cellulose**-based stabilizing agents
INVENTOR(S): Tuason, Domingo C., Bensalem, PA, United States
Selinger, Eugene B., Langhorne, PA, United States
Kravetz, Gregory R., Princeton Junction, NJ, United States
Sewall, Christopher, Hope, NJ, United States
Rogan, Daniel T., Yardley, PA, United States
PATENT ASSIGNEE(S): FMC Corporation, Philadelphia, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6391369	B1	20020521
APPLICATION INFO.:	US 1999-398627		19990917 (9) <---

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-135600P	19990524 (60) <---
	US 1999-151691P	19990825 (60) <---

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Khat, Nina
LEGAL REPRESENTATIVE: FMC Corporation
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 753
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention describes the use and preparation of a novel rapidly peptizable stabilizing composition comprising attrited colloidal microcrystalline **cellulose** wetcake coprocessed and dried with iota-carrageenan, and its use for stabilizing aqueous foods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Rapidly peptizable microcrystalline **cellulose**-based stabilizing agents

AB The present invention describes the use and preparation of a novel rapidly peptizable stabilizing composition comprising attrited colloidal microcrystalline **cellulose** wetcake coprocessed and dried with iota-carrageenan, and its use for stabilizing aqueous foods.
SUM0 This invention relates to rapidly peptizable stabilizing agents comprising microcrystalline **cellulose** and iota carrageenan. More particularly it relates to stabilizing agents comprising these two components which may be readily peptized in . . .
SUM0 Attempts have been made in the past to develop improved microcrystalline **cellulose**-based stabilizing agents for use in dry mix applications such as instant cocoa mix drinks and low fat or fat-free sauces . . . . with a barrier material. Several materials are mentioned for this purpose, but the most effective is stated to be sodium **carboxymethylcellulose** (CMC). The patent states (at column 5) that **methylcellulose**, hydroxypropyl **methylcellulose**, guar gum, alginates, esters, surfactants, and other hydrocolloids may have a slight barrier

L57 ANSWER 36 OF 79 USPATFULL on STN (Continued)
action when added in appreciably higher proportions. . . sucrosefal as a barrier coating, it is not universally accepted as a food ingredient because it is a chemically modified **cellulose** derivative rather than a natural ingredient.

SUMM It has been found that stabilized microcrystalline **cellulose** and iota carrageenan can be coprocessed at ratios between 80:20 and 50:50, respectively, in an aqueous slurry at or above. . .

SUMM . . . of this invention there is provided a process to prepare the coprocessed compositions of this invention by first attiting hydrolyzed **cellulose** wetcake, dispersing the attirited wetcake in water heated to above the temperature at which the particular grade of iota carrageenan being used dissolves, adding the dry carrageenan to the dispersion of microcrystalline **cellulose**, shating the components, equalizing the mixture to assure intimate mixing, and drying the dispersion.

SUMM . . . Pat. No 5,761,569, which does not provide any barrier coating properties at levels up to 70 weight % galactomannan gum, **carrageenan** provides barrier **coating** properties at levels as low as 20 weight % of the composition. A second consumption derives its functionality from the. . .

SUMM The microcrystalline **cellulose** employed in preparing the compositions of this invention is hydrolyzed **cellulose** wetcake which has been attirited to provide colloidal particles of MCC. For purposes of this invention colloidal is intended to. . . in the absence of iota carrageenan because this type of carrageenan interferes with the attrition by reducing the interaction between **cellulose** particles required to **release** the **cellulose** crystallites.

SUMM . . . anlfate content of iota carrageenan may range from about 25% to

34%, preferably about 32%, which is intermediate between kappa **carrageenan** which has a **25**% and lambda **carrageenan** which has a 35% water sulfate content. The sodium salt of iota carrageenan is soluble in

water, but different grades. . .

SUMM The useful ratios of attirited MCC to iota carrageenan range from about 80:20 to 50:50, respectively. To have adequate **carrageenan** present for barrier **coating** properties, the minimum level of **carrageenan** must be at least about 20 weight % on a dried solids basis, about 70 weight % MCC and 30 weight %.

SUMM The process to prepare the compositions of this invention begins with the attrition of hydrolyzed **cellulose** wetcake. As described above, the hydrolyzed **cellulose** wetcake is normally produced by the acid hydrolysis of wood pulp to partially depolymerize the **cellulose**, cleaving the **cellulose** chains in the amorphous regions, but leaving crystalline portions, called crystallites, hydrogen bonded to each other. The attrition is a mechanical step in which the partially depolymerized **cellulose** is placed under high shear in a variety of environments, e.g., Waring blenders, ball mills, planetary mixers, or other appropriate mechanical means. During the attrition process, the **cellulose** particles rub against each other, and the ensuing friction causes the individual crystallites to be separated or "peeled" from the fibers or fragment, freeing the crystallites. After attrition, the colloidal **cellulose** is dispersed in an appropriate amount of water that has been heated to a temperature at or above the dissolution

L57 ANSWER 36 OF 79 USPATFULL on STN (Continued)
temperature of the iota carrageenan with which it is to be coprocessed. For example, a satisfactory temperature of the **cellulose** dispersion would be approximately 57° C. when an iota carrageenan having an aqueous dissolution temperature of 50° C. is being used. The dry carrageenan is then added to the **cellulose** dispersion with agitation to dissolve the carrageenan. After the carrageenan has been completely dissolved, the dispersion is homogenized to assure. . .

SUMM . . . ultimately produces a microcrystalline powder. One such method is spray drying, a method which is frequently used to produce microcrystalline **cellulose** and microcrystalline **cellulose** coprocessed with, for example, **carboxymethylcellulose** or galactomannans. An alternate method to spray drying is the following steps. First, one or two volumes of alcohol, e.g., 95%

SUMM . . . high concentrations of salt and freeze/thaw stability in frozen desserts. These are properties not previously provided by a single microcrystalline **cellulose** composition. Examples are, for example, the materials described in U.S. Pat. No. 5,366,742 (Avicel® MC) have ready dispersibility provided there is. . .

SUMM . . . additional stabilizer is thus avoided by the use of the stabilizers of this invention. For example, at a use level of **25**% Avicel® MC/**carrageenan** stabilizer can successfully replace 2.5% of an MCC/CMC product (Avicel® CL-611) which required 9.4% of xanthan gum to be present. . .

SUMM . . . pork ice cream with improved creaminess and texture. Other possible uses include cosmetic creams, lotions, toothpaste, paints, polishing agents, and pharmaceutical and pesticide formulations as a suspending aid.

DETD . . . a large beaker containing 2529.9 grams of deionized water heated to 57° C., 389.8 grams of colloidal, i.e., attrited, microcrystalline **cellulose** wetcake (56.9% water content) was dispersed with a Lightnin' mixer fitted with a propeller stirrer. After dispersion

was complete, 80.3 grams of iota **carrageenan** (**100**% soluble at 50° C., water content 10.3%) was added to the dispersion. Upon complete dissolution of the carrageenan, the dispersion. . .

DETD . . . the preparation of a model sauce compising 10 grams of sodium chloride and **10** grams of MCC/**carrageenan** coprocessed with 90 grams of wetcake and. . . This mixture was easily dispersed cold with a wire whisk and was then.

DETD By the method of Example 1 551.7 grams of colloidal microcrystalline **cellulose** wetcake was dispersed in 2638.1 grams of deionized water, and 63.4 grams of iota carrageenan (5.38 water content) was added to. . . dispersion was 8500 cps (Brookfield RVF, spindle #4, 20 rpm. The spray-dried powder that was produced had a ratio of MCC/**carrageenan** of 80/**20**.

DETD By the method of Example 1 206.9 grams of colloidal microcrystalline **cellulose** wetcake was dispersed in 2695.1 grams of deionized water, and 95.0 grams of iota **carrageenan** (**10**% water content) was added to the resulting dispersion. After homogenization, the viscosity of the dispersion was 3000 cps (Brookfield RVF, . . .

DETD . . . a large beaker containing 2529.9 grams of deionized water heated to 57° C., 389.8 grams of colloidal, i.e., attrited, microcrystalline **cellulose** wetcake (56.9% water content) was dispersed

L57 ANSWER 36 OF 79 USPATFULL on STN (Continued)
with a Lightnin' mixer fitted with a propeller stirrer. After dispersion

was complete, 80.3 grams of iota **carrageenan** (**100**% soluble at 50° C., water content 10.3%) was added to the dispersion. Upon complete dissolution of the carrageenan, the dispersion. . .

DETD . . . in Example 5C the stabilizer is MicroGuick® MC-595, a commercial MCC-based stabilizer system. Cheese sauce formulations are detailed in Table **2**. Dispersion of MCC/**carrageenan** in either milk or water required 10-15 minutes whereas the MicroGuick® MC-595 required 15-20 minutes for full dispersion.

DETD . . . 0.18 0.18

.sup.aNI, L. J. Minor
.sup.bIP 193, National Starch and Chemical Corp
.sup.cLand O' Lakes
.sup.dMCC/**Carrageenan** (70:30), Example 1
.sup.eMicroQuick ® MC-595, FMC Corporation
DETD . . . of sugar, 310 grams of non-fat dry milk solids, 322.5 grams of corn syrup solids, 50 grams of maltodextrin (M-150), **25** grams of MCC/**Carrageenan** (70:30, prepared in Example 1), 25 grams of vanilla powder, 7 grams of **carboxymethylcellulose** (Aqualon® 7HF, Hercules, Incorporated), and 0.5 gram of carrageenan (Viscarin® SC 3920, FMC Corporation) was thoroughly mixed. In a large. . .
DETD . . . 25.sup.a 20.sup.b
Maltodextrin 50 50
Carrageenan.sup.c 0.5 1
CMC.sup.d 7 8.5
Vanilla powder 25 25
Viscosity (cps) 640 550

.sup.aMCC/**carrageenan** (70:30), Example 1
.sup.bAvicel ® CL-611 FMC Corporation)
.sup.cViscarin ® SC 3920, FMC Corporation
.sup.dAqualon ® 7HF, Hercules, Incorporated
DETD . . . 3.00 1.00
Gelatin.sup.a 3.00 5.0
Starch.sup.a 1.00 2.00
Cultured yogurt.sup.a 36.80 36.20 37.30 38.3
Physical properties
pH.sup.a 4.18 4.18 4.18 4.40
Viscosity (cps).sup.a 2100 1750 3100 1500

.sup.aMCC/**carrageenan** (70:30), Example 1
.sup.bGelatin 250 B
.sup.cThin-N-Thik ®, National Starch and Chemical Corporation
.sup.dLive culture yogurt, Dannon Co. Inc. Farm ®
After 4 hours incubation and. . .
DETD . . . 2.05
EDTA, calcium disodium 0.025 0.025
Beta carotene 0 .060 0.025

.sup.aFurkity ® 49, National Starch and Chemical Corporation
.sup.bMCC/**carrageenan** (70:30), Example 1
.sup.cAvicel ® CL-611, FMC Corporation
.sup.dHydrogenated soybean oil
.sup.eEgg flavor 729015.007, Firmenich, Inc.
.sup.fLemon flavor 550.14726, . . .
DETD In a 250 mL beaker were placed 98 grams of commercial soy sauce

L57 ANSWER 36 OF 79 USPATFULL on STN (Continued)
(Kikkoman, about.24 weight % salt) and **2** grams of MCC/**carrageenan** stabilizer (70:30, prepared in Example 1). This mixture was stirred with

a Lightnin' mixer fitted with a propeller blade operated. . . turmeric was prepared. Simultaneously, in a large Waring blender operated at high speed were placed 3675 grams of water and 100 grams of MCC/**carrageenan** stabilizer (70:30, prepared in Example 1) for a 5 minute period. This dispersion was transferred to a large vessel. Then, . . . and 30.0, respectively, of the 118 ml of emulsifiers were uniform texture than Example 11B as well as much better flavor **release**.

DETD . . . 1.0

.sup.aPurity ® W, National Starch and Chemical Corporation
.sup.bMelogel ®, National Starch and Chemical Corporation
.sup.cMCC/**carrageenan** (70/30), Example 1
.sup.dFidoo Industrial Division, Food Ingredient Specialties, Inc.
.sup.eGB Select Mushroom Type Flavor, Gist-brocades
.sup.fMid-America Farms
.sup.gSilitrol . . . not include flavorings and herbs, but does include the ingredients which affect stability and can be dispersed by dispersing **15** grams of MCC/**carrageenan** (70:30, prepared in Example 2) in 542.40 grams of deionized water using a Lightnin' mixer fitted with a propeller blade. . .

DETD . . . sugar, 26.8% grams of non-fat milk solids, 4 grams of high viscosity guar (FG 60-70), and 3 grams of microcrystalline **cellulose**/iota **carrageenan** (70:30, Example 1) was prepared and thoroughly mixed. This dry blend was added to 933.14 grams of 2% milk which was stirred with.

CLM What is claimed is:
1. A dried composition comprising coprocessed colloidal microcrystalline
cellulose and iota carrageenan, said carrageenan having a dissolution temperature in water no higher than 80° C., wherein the weight ratio of microcrystalline **cellulose** to iota carrageenan is in the range from 80:20 to 50:50, respectively.

CLM What is claimed is:
2. A composition of claim 1 wherein the weight ratio of colloidal microcrystalline **cellulose** to iota carrageenan is 70:30.

CLM What is claimed is:
3. A composition of claim 1 wherein the weight ratio of colloidal microcrystalline **cellulose** to iota carrageenan is 50:50.

CLM What is claimed is:
4. A composition of claim 1 wherein the iota **carrageenan** is soluble in water at 50° C.

CLM What is claimed is:
5. A process for preparing a composition of claim 1 comprising the following steps: (a) subjecting hydrolyzed **cellulose** to attrition to make colloidal microcrystalline **cellulose**; (b) dispersing said colloidal microcrystalline **cellulose** in water heated to a temperature above the solubility temperature of the dry iota carrageenan to be coprocessed with said colloidal microcrystalline **cellulose**; (c) adding said dry iota carrageenan to said heated dispersion of colloidal microcrystalline **cellulose** and mixing the components, creating a

L57 ANSWER 36 OF 79 USPATFULL on STN (Continued)
slurry; (d) homogenizing said slurry; and (e) drying said slurry to produce a copreomead. . .

L57 ANSWER 37 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2002:115771 USPATFULL
TITLE: Microcapsule and method of making the same
INVENTOR(S): Miyazawa, Kazuyuki, Yokohama, JAPAN
Kaneda, Isamu, Yokohama, JAPAN
Yanaki, Toshio, Yokohama, JAPAN
PATENT ASSIGNEE(S): Shiseido Co., Ltd., Tokyo, JAPAN (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6391288	B1	20020521	
APPLICATION INFO.:	US 2000-625504		20000726 (9)	<--

	NUMBER	DATE	
PRIORITY INFORMATION:	JP 1999-212373	19990727	<--
	JP 2000-09742	20000328	<--
	JP 2000-09743	20000328	<--
	JP 2000-09744	20000328	<--
	JP 2000-09745	20000328	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Dees, Jose' G.
ASSISTANT EXAMINER: Lum, Nicina
LEGAL REPRESENTATIVE: Chao, Fei-Fei, Venable
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 1956
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A microcapsule of the present invention is characterized in that it encapsulate oil droplets having average particle size of 0.01 to 3 um and its capsulating agent is a hydrophilic polymer gelling agent. The main component of the capsulating agent is preferably a hydrophilic polymer gelling agent which hardens by heating and cooling, and, in particular, agar or carrageenan. In the making method of the present invention, a microcapsule can be made efficiently due to no loss in the inner oil phase, and its particle size can easily be controlled. The microcapsule is excellent in shearing-resistance, store stability. Also,
if the fracture strength of the microcapsule is within a specific range,
a microcapsule which releasing characteristic of encapsulated oil droplets when applied is immediately, gradually or non-releasing can be obtained. Further, when such a hydrophilic microcapsule is coated, the contraction in air, dispersibility to various medium, and elusion of
encapsulated components in medium can be also improved.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . hydrophilic gel. Examples thereof include proteins such as gelatin or collagen, and polysaccharides such as agar, carrageenan,

L57 ANSWER 37 OF 79 USPATFULL on STN (Continued)
glucomannan, scleroglucan, schizophyllan, **gellan gum**, alginic acid, curdle, pectin, hyaluronic acid, or guar gum.
DETD Also, if necessary, other hydrophilic polymers, for example, such as synthetic polymers like polyacrylic acid, carboxymethyl cellulose, and cationized **cellulose**; and natural polymers such as xanthan gum and locust bean gum can be used within a range which does not . . .
DETD . . . acid, palmitic acid, stearic acid, or behenic acid; higher alcohols such as lauryl alcohol, cetanol, oleyl alcohol or stearyl alcohol; **microcellulose**; polyacrylate copolymer; highly polymerized methylpolysiloxane; and the like.
DETD Examples of amphiphilic coating agent include allylated polysaccharides such as ethyl **cellulose**, propyl **cellulose**, hydroxyethyl **cellulose**, hydroxypropyl **cellulose**, ethylhydroxyethyl **cellulose** or allylated xanthan gum; polyacrylic acid-polyacrylate copolymer; and the like.
DETD Examples of hydrophilic coating agent include polymers such as **polyvinyl** alcohol, **polyvinyl** pyrrolidone or cationized **cellulose**; polysaccharides such as gtumes or sucroes; and the like.
DETD . . . hydrophilic microcapsule is agar, carrageenan, or the like, examples of particularly preferred coating agents include hydrophobic polysaccharides such as ethyl **cellulose**, propyl **cellulose**, hydroxyethyl **cellulose**, hydroxypropyl **cellulose**, ethylhydroxyethyl **cellulose**, and alkylated xanthan gum.
DETD

Polyvinyl alcohol 15 wt %
Carboxymethyl **cellulose** 5
1,3-Butylene glycol 5
Ethanol 5
POE oleyl alcohol 0.5
Microcapsule(Compounding Example 1-2) 10
Ion-exchanged. . .
DETD

(1)1,3-Butylene glycol 15 wt %
(2)**Polyvinyl** alcohol 5
(3)Microcapsule(Compounding Example 1-2) 50
(4)Ethanol 10
(5)PEG 6000 3
(6)PEG 1200 2
(7)POE(25). . .
DETD
Water phase:
(8) 1,3-Butylene glycol 10
(9) POE(60) hardened castor oil 1
(7) Agar(AS-100) 1
(8) **Gellan gum** 0.3
(9) Citric acid 0.1
(10)Sodium citrate 0.1
(11)Ascorbic acid 2-glucoside 2.5
(12)Ion-exchanged water 24.0
. .
DETD

(1)Dipropylene glycol 7 wt %
(2)Polyethylene glycol 1500 8
(3)Carboxyvinyl polymer 0.4
(4)Methyl **cellulose** 0.2
(5)POE(15) oleyl ether 1

L57 ANSWER 37 OF 79 USPATFULL on STN (Continued)
(6)Potassium hydroxide 0.1
(7)Microcapsule(Example1-1) 1
(8)Purified water 82.3
(9)Perfume Q.S.
DETD

Polyvinyl alcohol 15 wt %
Carboxymethyl **cellulose** 5
1,3-Butylene glycol 5
Ethanol 5
POE oleyl alcohol 0.5
Microcapsule(Compounding Example II-2) 10
Ion-exchanged. . .
DETD

(1)1,3-Butylene glycol 15 wt %
(2)**Polyvinyl** alcohol 5
(3)Microcapsule(Compounding Example II-2) 50
(4)Ethanol 10
(5)PEG 6000 3
(6)PEG 1200 2
(7)POE(25). . .
DETD
Water phase:
(8) 1,3-Butylene glycol 10
(9) POE(60) hardened castor oil 1
(7) Agar(I-1) 1
(8) **Gellan gum** 0.3
(9) Citric acid Q.S.
(10)Sodium chloride 0.1
(11)Ascorbic acid 2-glucoside 2.5
(12)Ion-exchanged water Balance
. .
DETD

(1)Dipropylene glycol 7 wt %
(2)Polyethylene glycol 1500 8
(3)Carboxyvinyl polymer 0.4
(4)Methyl **cellulose** 0.2
(5)POE(15) oleyl ether 1
(6)Potassium hydroxide 0.1
(7)Microcapsule(Example II-1) 1
(8)Purified water 82.3
(9)Perfume. . .
DETD
TABLE 17

Coating agent'
Solid paraffin 5 — — — —
Highly polymerized methyl polysiloxane — 2 — —
Ethyl **cellulose** — — 1 —
Contraction State
Immediately after filtrating .largecircle. .largecircle. .largecircle. .largecircle.
After drying .largecircle. .largecircle. .largecircle. X
Elution of AZO(%) 0 0. . . .
DETD . . . evaluation of microcapsules coated with lipophilic coating agents (solid paraffin, highly polymerized methyl polysiloxane) or an

L57 ANSWER 37 OF 79 USPATFULL on STN (Continued)
amphiphilic coating agent (ethyl **cellulose**). From TABLE 17, it can be seen that these coatings suppress the contraction of microcapsules in air, and improve the. . .

DETD
TABLE 18

Coating agent*
Solid paraffin 5 -- -- --
Highly polymerized methyl polysiloxane -- 2 -- --
Methyl **cellulose** -- -- 1 --
Dispersibility**
Cotyl sebacate containing solid paraffin ,largecircle. ,largecircle. ,circleincircle. A
Methyl polysiloxane(20 cps) containing
highly polymerized methyl polysiloxane ,circleincircle. ,circleincircle. ,largecircle. A
Cotyl sebacate containing ethyl **cellulose** ,largecircle. ,largecircle. ,circleincircle. A

*Adding amount (g) of the coating agent per 100 g of microcapsule oily dispersion
**Each concentration of. . .
DETD
TABLE 19

Coating agent*
Polyvinyl alcohol 5 1 --
Centrifugation State
Immediately after filtrating ,largecircle. ,largecircle. ,largecircle.
After drying ,largecircle. A A
Elution of A20(4) 0 0 10
Dispersability
Water ,circleincircle. ,circleincircle. ,largecircle.
Water containing **polyvinyl** alcohol** ,circleincircle. ,circleincircle. ,largecircle.

*Adding amount (g) of the coating agent per 100 g of microcapsule oily dispersion
The concentration of **polyvinyl alcohol in water was 10 wt %.
DETD Non-**coated** microcapsules were prepared by using **carrageenan** in the place of agar in the non-coated microcapsule of Test Example IV-1, and collected by filtration. 10 g of thus obtained microcapsules were added to a mixture of 5 g of **polyvinyl** alcohol, 5 g of acrylic acid-alkyl acrylate copolymer, 70 g of purified water, and 20 g of ethanol. After being. . .

DETD

Dipropylene glycol 7 wt %
PEG 1000 8
Methyl **cellulose** 0.2
POE(15) oleyl ether 1
Potassium hydroxide 0.1
Coated microcapsule(Manufacturing Example IV-3) 5
Purified water 78.3

L57 ANSWER 38 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2002:49597 USPATFULL
TITLE: Enteric coated microgranules for stabilizing lactic acid bacteria
INVENTOR(S): Kim, Dong Yeon, Seoul, KOREA, REPUBLIC OF
Park, Dong Woo, Seoul, KOREA, REPUBLIC OF
Jeon, Sang Hyeol, Suwon-shi, KOREA, REPUBLIC OF
PATENT ASSIGNEE(S): Il Yang Pharm. Co., Ltd., Seoul, KOREA, REPUBLIC OF (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6345149	B1	20020402	
	WO 9920129		19990429	
APPLICATION INFO.:	US 2000-529354		20000414	(9) <--
	WO 1998-KR380314		19981026	
			20000414	PCT 371 date

	NUMBER	DATE	
PRIORITY INFORMATION:	KR 1997-53312	19971017	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Weber, Jon P.
ASSISTANT EXAMINER: Patten, Patricia A.
LEGAL REPRESENTATIVE: Cordas, Peter F., O'Day, Christine C., Edwards & Angell, LLP
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 678
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to an enteric coated granule prepared by coating lactic acid bacteria-containing seed with a water-miscible coating material and then, if desired, subjecting the first coated product to the second coating with a controlled-release coating material.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AI 19991016
20000414 PCT 371 date

SUMM . . . the intestine by using more than 10 times excess of bacteria has been proposed in the field of food and **pharmaceutical** industry. However, it is not a fundamental solution, but merely a very fragmentary and waiting, temporary remedy. Further, food containing. . . the gastric or intestinal juice. Further, numerous organic solvent-based coating methods utilizing various polymers have been reported in the general **pharmaceutical** field (see, PCT/US94/00167, Japanese Patent Appln. Kea 91-235667, 92-364123, 92-41434, 93-186335, 93-186336, etc.). However, such coating techniques are not satisfactory. . . .

SUMM . . . extract, alginic acid, polymethylmethacrylate (Eudragit L30D, Eudragit L230D, Rollicoat MAE 30D (manufactured by BASF Co.), etc.), wheat protein, soybean protein, **methylcellulose** (MC),

L57 ANSWER 37 OF 79 USPATFULL on STN (Continued)
Antiseptic Q.S.
Coloring agent. .
IT 56-81-5, Glycerin, biological studies 57-13-4, Stearic acid, biological studies 79-81-2, Vitamin A palmitate 107-88-0, 1,3-Butylene glycol 110-27-0, Isopropyl myristate 111-01-3, Squalane 122-83-3, Dicetyl sebacate 127-82-2, Zinc p-phenolsulfonate 541-82-4, Decamethylcyclopentasiloxane 556-67-2, Octamethylcyclotetrasiloxane 1314-13-2, Zinc oxide, biological studies 1727-41-9, Aluminum chlorohydrate 1758-41-9, Sorbitan sesquioleate 3382-94-7, Triclosan 7631-86-9, Silica, biological studies 9000-07-1, Carrageenan 9002-18-0, Agar 9016-00-6, Dimethylpolysiloxane 14097-96-0, Talcum, siliconized 25322-68-3D, Polyethylene oxide, copolymer with Me polysiloxane 31692-14-3, Ethyl p-alkoxybenzoate 56611-84-4, Sorbitan stearate 64429-25-4, Benton 78356-69-3 **71010-52-1, Gellan gum** 72585-97-8, Cetyl lanostanoate 129499-78-1, L-Ascorbic acid 2-glucoside
(method and hydrophilic polymer gelling agent for preparation of oil-containing microcapsules)
IT **71010-52-1, Gellan gum**
(method and hydrophilic polymer gelling agent for preparation of oil-containing microcapsules)

L57 ANSWER 38 OF 79 USPATFULL on STN (Continued)
hydroxypropylcellulose (HPC), **hydroxypropylmethylcellulose** (HPMC; **pharma** coat, aqua coat, etc.), **polyvinylacetatephthalate** (Sureteric; manufactured by Colorcon Co.), gums, for example, guar gum, locust bean gum, xanthan gum, **gellan gum**, arabic gum, etc. Since these water-miscible coating materials are water-soluble or water-dispersible,
it is advantageous that the first coating procedure. . .
SUMM As the second coating material, the controlled-release coating material,
particularly an enteric coating material commonly used in **pharmaceutical** field; or a coating material for swelling such as carbopol or arabic gum; and other controlled-release coating materials can be . . . sodium alginate, alginic acid, polymethylmethacrylate, for example, Eudragit L30D, Eudragit L30D, Rollicoat MAE 30D (manufactured by BASF Co.), etc., shellac, **hydroxypropylmethylcellulose** phthalate (HPMCP), **hydroxypropylmethylcellulose** (HPMC), hydroxy-**propylmethylcellulose**acetatesuccinate (HPMCAS), **carboxymethylcellulose** (CMC), **hydroxypropylcellulose** (HPC), **cellulose**acetatephthalate (CAP), **polyvinylacetatephthalate** (Sureteric;Colorcon Co.)), **ethylcellulose** (EC), **methylcellulose** (MC), soybean protein or wheat protein (they are registered as Food Additives), chitin, chitinic acid, agar, carrageenan, pectin, carbopol, or gums, such as for example, guar gum, locust bean gum, xanthan gum, **gellan gum**, arabic gum, etc. can be mentioned. Among them, one or more selected from the group consisting of corn protein extract, **hydroxypropylmethylcellulose** phthalate (HPMCP) and shellac are preferably used as the second coating material.
SUMM 95% by weight with respect to the first coated granule. Particularly, when the enteric coating material commonly used in the **pharmaceutical** field is used, it is used in an amount ranging from 1 to 40% by weight; or when other coating
CLM What is claimed is:
. . . water-miscible coating material is one or more selected from the group consisting of sodium alginate, polymethylmethacrylate, shellac, protein, soybean protein, **methylcellulose**, **hydroxypropylcellulose**, **hydroxypropylmethylcellulose**, polyvinylacetate phthalate, guar gum, locust bean gum, xanthan gum, **gellan gum** and arabic gum.

CLM What is claimed is:
. . . more selected from the group consisting of corn protein extract and processed materials thereof, sodium alginate, alginic acid, polymethylmethacrylate, shellac, **hydroxypropylmethylcellulose**phthalate, **hydroxypropylmethylcellulose**, **hydroxypropylmethylcellulose**acetatesuccinate, **carboxymethylcellulose**, **hydroxypropylcellulose**, **cellulose**acetatephthalate, **polyvinylacetatephthalate**, **ethylcellulose**, **methylcellulose**, soybean protein, wheat protein, chitin, chitinic acid, agar, carrageenan, pectin, carbopol, guar gum, locust bean gum, xanthan gum, **gellan gum** and arabic gum.

CLM What is claimed is:
7. The coated granule according to claim 6, wherein the controlled-release coating material is one or more selected from the group consisting of corn protein extract, **hydroxypropylmethylcellulose**phthalate and shellac.

IT 63-42-3, Lactose 299-28-5, Calcium gluconate 526-95-4, D-Gluconic

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acid 814-80-2, Calcium Lactate 1398-61-4, Chitin 9000-01-5, Arabic gum 9000-07-1, Carrageenan 9000-30-0, Guar gum 9000-60-2, Locust bean gum 9000-69-5, Pectin 9002-18-0, Agar 9002-32-4 9004-38-0, **Cellulose** acetate phthalate 9004-57-3, Ethylcellulose 9004-64-2, Hydroxypropylcellulose 9004-65-3, Hydroxypropylmethylcellulose 9004-67-5, Methylcellulose 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9005-38-3, Sodium alginate 9021-14-7, Polymethylmethacrylate 9050-36-6, Hydroxypropylmethylcellulose phthalate 11138-66-2, Xanthan gum 51237-58-6 **71210-52-1, Gellan gum** 71210-97-1, Hydroxypropylmethylcellulose acetate succinate 76050-42-5, Carbopol 940

(**coating** material; enteric coated microgranules for stabilizing lactic acid bacteria)

IT **9000-07-1**, Carrageenan **71210-52-1, Gellan gum**

(**coating** material; enteric coated microgranules for stabilizing lactic acid bacteria)

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profile. Such **release** rates can provide therapeutically effective levels of agent for an extended period of time and thereby provide a longer period of **pharmacologic** or diagnostic response as compared to conventional rapid **release** dosage forms. Such longer periods of response provide for many inherent benefits that are not achieved with the corresponding short acting, immediate **release** preparations. For example, in the treatment of chronic pain, controlled **release** formulations are often highly preferred over conventional short-acting formulations.

SUMM [0003] Controlled **release pharmaceutical** compositions and dosage forms are designed to improve the delivery profile of agents, such as drugs, nediaments, active agents, diagnostic agents, or any substance to be internally administered to an animal, including humans. A controlled **release** composition is typically used to improve the effects of administered substances by optimizing the kinetics of delivery, thereby increasing bioavailability, convenience, and patient compliance, as well as reducing side effects associated with inappropriate immediate **release** rates such as a high initial **release** rate and, if undesired, uneven blood or tissue levels.

SUMM 5,510,118, 5,134,370, and 4,826,689, which are specifically incorporated by reference. However, rapid dissolution is contrary to the

goal of controlled **release**. Known controlled **release** formulations do not present a solution to this problem.

SUMM [0006] Prior art teachings of the preparation and use of compositions providing for controlled **release** of an active compound provide various methods of extending the release of a drug following administration. However, none of the methods suggest a successful method of administering a nanoparticulate formulation.

SUMM [0007] Exemplary controlled **release** formulations known in the art include specially coated pellets, granules, tablets, implants, tablets, minitabs, and capsules in which a controlled **release** of a drug is brought about, for example, through selective breakdown of the coating of the preparation, through **release** through the coating, through compounding with a special matrix to affect the **release** of a drug, or through a combination of these techniques. Some controlled **release** formulations provide for pulsatile **release** of a single dose of an active compound at predetermined time after administration.

SUMM [0008] U.S. Pat. No. 5,120,685 to Acharya et al. refers to a calcium polycarbophil-alginate controlled **release** composition. U.S. Pat. No. 5,213,758 to Krishnamurthy et al. refers to a controlled **release** suppository composition of sodium alginate and pectin. U.S. Pat. No. 5,911,389 to Friend et al. refers to a solid alginate-based formulation including alginate, a water-swellable polymer, and a digestible hydrocarbon derivative for providing controlled **release** of orally administered compounds.

SUMM [0009] WO 91/19512 refers to the sustained **release** of **pharmaceuticals** using compositions in which the drug is complexed with an ion-exchange resin. The specific ion-exchange resin described in this

published

SUMM [0010] U.S. Pat. No. 5,811,425 to Woods et al. refers to injectable depot forms of controlled **release** drugs made by forming microencapsule matrices of the drug in biodegradable polymers, liposomes, or microemulsions compatible with body tissues. U.S. Pat. No. 5,811,425 to Lan et al. refers to controlled **release** compositions obtained by coupling a class of drugs to biodegradable polymers, such as polylactic acid, polyglycolic acid, copolymers of polylactic. . .

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ACCESSION NUMBER: 2002:213540 USPATFULL
TITLE: CONTROLLED-**RELEASE** NANOPARTICULATE COMPOSITIONS
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described are controlled **release** nanoparticulate formulations comprising a nanoparticulate agent to be administered and a rate-controlling polymer which functions to prolong the **release** of the agent following administration. The novel compositions **release** the agent following administration for a time period ranging from about 2 to

about 24 hours or longer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI CONTROLLED-**RELEASE** NANOPARTICULATE COMPOSITIONS

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about 24 hours or longer.

SUMM [0001] The present invention relates to controlled **release** compositions containing a poorly soluble agent such as a drug. In particular, the present invention relates to compositions in which. .

SUMM [0002] Controlled **release** refers to the **release** of an agent such as a drug from a composition or dosage form in which the agent is **released** according to a desired profile over an extended period of time. Controlled **release** profiles include, for example, sustained **release**, prolonged **release**, pulsatile **release**, and delayed **release** profiles. In contrast to immediate **release** compositions, controlled **release** compositions allow delivery of an agent to a subject over an extended period of time according to a predetermined

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. . . to De Kruss et al. refers to the use of liposomes having prolonged circulation half-lives to provide for the sustained **release** of drug compositions.

SUMM [0012] Nanoparticulate compositions addressed a need in the art for **pharmaceutically**-acceptable compositions containing poorly-water soluble agents. However, the known nanoparticulate compositions are not suitable for controlled-**release** formulations. There remains a need in the art for controlled **release** nanoparticulate compositions.

SUMM [0013] This invention is directed to the surprising and unexpected discovery of new controlled **release** nanoparticulate compositions. The controlled **release** compositions provide for the therapeutically effective **release** of an incorporated drug or other substance in a patient for a time period ranging from about 2 to about 24

SUMM [0014] The controlled **release** nanoparticulate compositions comprise a nanoparticulate drug or other agent to be administered, such as a crystalline or amorphous nanoparticulate drug. . . . at least one surface stabilizer associated with the surface of the nanoparticulate drug or other agent. In addition, the controlled **release** nanoparticulate composition comprises one or more **pharmaceutically** acceptable rate-controlling polymers, which function to prolong **release** of the administered nanoparticulate drug or agent thereby resulting in controlled **release**. Optionally, one or more auxiliary excipient materials can also be included in the controlled **release** composition.

SUMM [0015] Controlled **release** compositions according to this invention containing a nanoparticulate form of a poorly soluble drug are advantageous in that the improved

SUMM [0016] Preferably, the effective average particle size of the nanoparticulate agent prior to inclusion in the controlled **release** nanoparticulate composition is less than about 1000 nm, less than about 800 nm, less than about 600 nm, less than

SUMM [0017] The present invention also provides dosage forms for the controlled **release** compositions as described above in tablet form or in wettalpatticate form to be administered in any conventional method, such as. . . .

SUMM . . . surface stabilizer, the rate controlling polymer material, and one or more auxiliary excipients are compressed together to form a controlled **release** matrix. The controlled **release** matrix may optionally be coated with a rate controlling polymer so as to provide additional controlled **release** properties.

SUMM . . . tablet. The multilayer tablet may optionally be coated with a rate controlling polymer material so as to provide additional controlled

release properties. In an alternative aspect, a first layer in such a multilayer tablet comprises controlled **release** composition according to the invention and a second layer comprises a conventional active ingredient containing composition, such as an instant **release** composition.

SUMM . . . tablets. The compressed multiparticulate tablet may optionally be coated with rate controlling polymer material so as to provide additional controlled **release** properties.

SUMM [0024] The present invention further relates to processes for the manufacture of controlled **release** compositions in which a poorly soluble drug or other agent is present in nanoparticulate form. In one aspect, the method. . . comprising a poorly soluble drug or other agent to be administered and a surface stabilizer; (2) adding one or more **pharmaceutically** acceptable rate-controlling polymers; and (3) forming a solid dose form of the composition for administration. . .

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Pharmaceutically acceptable excipients can also be added to the composition for administration. Methods of making nanoparticulate compositions, which can comprise mechanical

SUMM . . . method of treating a mammal, including a human, requiring extended administration of a drug or other agent with a controlled **release** nanoparticulate composition of the invention which **releases** an incorporated drug or other agent providing a desired effect for a period from about 2 to about 24 hours or longer. The controlled **release** nanoparticulate composition can be administered in any conventional method, such as via oral, rectal, buccal, and vaginal routes.

BRWD [0027] FIG. 1: Shows a graph of the cumulative % drug (naproxen) **released** over time using a nanoparticulate composition comprising 30% Pluronic® **hydroxypropylcellulose** (HPC) and 2% **polyvinylpyrrolidone** (PVP);

BRWD [0028] FIG. 2: Shows a graph of the cumulative % drug (naproxen) **released** over time for three different nanoparticulate compositions having a hardness of 15, 22, and 25 kp;

BRWD [0029] FIG. 3: Shows a graph of the cumulative % drug (naproxen) **released** over time for nanoparticulate compositions using different types of hydroxypropyl **methylcellulose** (HPMC);

BRWD [0030] FIG. 4: Shows a graph of the cumulative % drug (naproxen) **released** over time for nanoparticulate compositions comprising one of six different types of HPMC;

BRWD [0031] FIG. 5: Shows a graph of the cumulative % drug (naproxen) **released** over time for nanoparticulate compositions having varying amounts Lubritab® (a hydrogenated vegetable oil);

BRWD [0032] FIG. 6: Shows a graph of the cumulative % drug (naproxen) **released** over time for a spray-dried nanoparticulate formulation and a formulation of blended raw drug and stabilizer;

BRWD [0033] FIG. 7: Shows a graph comparing the cumulative % drug (naproxen) **released** over time for nanoparticulate formulations comprising different concentrations of Methocel® K100LV (HPMC);

BRWD [0034] FIG. 8: Shows a graph comparing the cumulative % drug (naproxen) **released** over time for directly compressed and wet granulated nanoparticulate formulations of Zein® and Methocel®; and

BRWD [0035] FIG. 9: Shows the controlled **release** of nanoparticulate nifedipine from directly compressed Methocel® tablets.

BRWD . . . the mean in vivo plasma profiles of nifedipine after single dosed, fasted, administration in humans for (1) nifedipine containing controlled **release** matrix tablets coated with a controlled **release** coating according to the present invention as described in Example 12; and (2) a control composition.

BRWD . . . the mean in vivo plasma profiles of nifedipine after single dosed, fasted, administration in humans for (1) a nifedipine controlled **release** composition manufactured according to the present invention as described in Example 14; and (2) a control composition.

DETD A. CONTROLLED **RELEASE** NANOPARTICULATE COMPOSITIONS

DETD [0038] This invention is directed to the surprising and unexpected discovery of new solid controlled **release** nanoparticulate compositions. It is expected that the controlled **release** compositions provide effective blood levels of an incorporated drug or other agent in a patient for an extended period. . . . rapid dissolution of the drug or other agent following administration. Rapid

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excipients and are described in detail in the Handbook of **Pharmaceutical** Excipients, published jointly by the American **Pharmaceutical** Association and The **Pharmaceutical** Society of Great Britain (The **Pharmaceutical** Press, 1986), specifically incorporated by reference.

DETD [0055] The present invention identifies **pharmaceutically** acceptable rate-controlling polymers for use in the present rate-controlling polymer material that unexpectedly provide excellent controlled **release** properties for nanoparticulate compositions. Rate-controlling polymers include hydrophilic polymers, hydrophobic polymers, and mixtures of hydrophobic and hydrophilic polymers that are capable of retarding the **release** of a drug compound from a composition or dosage form of the present invention.

DETD [0056] Particularly useful rate-controlling polymers for causing an effective controlled **release** of nanoparticulated drug or other agent following administration include plant exudates (gum arabic), seaweed extracts (agar), plant seed gums (psyllium), modified plant starches (cornstarches),

cellulosics such as hydroxypropyl **cellulose** (HPC), hydroxyethyl **cellulose** (HEC), hydroxypropylmethyl cellulose (HPMC), and sodium **carboxymethylcellulose** (CMC), guar, pectin, and carrageenan.

Additional polymers contemplated for use herein are **cellulose** such as ethyl **cellulose** and methyl **cellulose**, carboxymethyl **cellulose**, hydrophilic **cellulose** derivatives, polyethylene glycol, **polyvinylpyrrolidone**, **cellulose** acetate, **cellulose** acetate butyrate, **cellulose** acetate phthalate, **cellulose** triinellitate, **polyvinyl** acetate phthalate, hydroxypropylmethyl **cellulose** phthalate, hydroxypropylmethyl **cellulose** acetate succinate, **polyvinyl** acetaldiethylamino acetate, polyalkylmethacrylate and copolymers of acrylate. Other suitable hydrophobic polymers include polymers and/or copolymers derived from acrylic or methacrylic acid

D 3. Other **Pharmaceutical** Excipients

DETD [0057] **Pharmaceutical** compositions according to the invention may also comprise one or more auxiliary excipients such as binding agents, diluents, lubricating agents, . . . choice of excipients and their relative amounts will depend on factors such as the particular route into which the controlled **release** composition is incorporated.

DETD [0058] Suitable diluents are those **pharmaceutically** acceptable inert fillers such as microcrystalline **cellulose**, lactose, dibasic calcium phosphate, saccharides, and/or mixtures of any of the foregoing. Examples of diluents include microcrystalline **cellulose** such as Avicel PH101, Avicel PH102, Avicel PH200, lactose such as lactose monohydrate, lactose anhydrous, and **Pharmatose** DCL21; dibasic calcium phosphate such as Emcompress; mannitol; starch; sorbitol; sucrose; and glucose. The diluent, if present, is preferably used.

DETD [0059] Examples of binding agents are various **cellulose**s and cross-linked **polyvinylpyrrolidone**.

DETD [0060] Suitable disintegrants include lightly crosslinked **polyvinyl** pyrrolidone, corn starch, potato starch, maize starch, and modified starches, croscarmellose sodium, cross-povidone, sodium starch glycolate, and mixtures thereof.

DETD [0064] The relative amount of nanoparticulate agent in the controlled **release** compositions of the invention can vary widely and can depend upon, for example, the agent selected for controlled **release** delivery. The poorly soluble drug or **pharmaceutically** acceptable salt thereof

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dissolution is generally contrary to the goal of controlled **release** formulations.

DETD [0039] As used herein, "controlled **release**" means the **release** of an agent such as a drug from a composition or dosage form in which the agent is **released** according to a desired profile over an extended period of time, such as from about 2 to about 24 hours or longer. **Release** over a longer time period is also contemplated as a "controlled **release**" dosage form of the present invention.

DETD [0040] The solid dose controlled **release** nanoparticulate compositions of the invention comprise a therapeutic or comprise nanoparticulate drug or other agent to be administered, having an . . .

DETD [0042] The nanoparticles of the invention comprise a therapeutic agent, diagnostic agent, or other agent to be administered for controlled **release**. A therapeutic agent can be a drug or **pharmaceutical**, and a diagnostic agent is typically a contrast agent, such as an x-ray contrast agent, or any other type of agent.

DETD [0044] Suitable drugs or diagnostic agents include those intended for controlled **release** delivery. Preferable drug classes **include** those that have short half-lives for clearance.

DETD . . . diuretics, dopaminergics (antiparkinsonian agents), . . . hemostatics, immunological agents, lipid regulating agents, muscle relaxants, parasympathomimetics, parathyroid calcitonin and bisphosphonates, prostaglandins, radio-**pharmaceuticals**, hormones, sex hormones (including steroids), anti-allergic agents, stimulants and anoretics, sympathomimetics, thyroid agents, vaccines, vasodilators, and xanthines.

DETD . . . and diagnostic agents and a listing of species within each class can be found, for instance, in Martindale, The Extra **Pharmacopoeia**, Twenty-ninth Edition (The **Pharmaceutical** Press, London, 1989), specifically incorporated by reference. The agents or diagnostic agents are commercially available and/or can be prepared by . . .

DETD . . . naproxen, nicergoline, nifedipine, norfloxacin, omeprazole, paclitaxel, phenytoin, piroxicam, quinagrel, ramipril, rosiglitazone, sertraline, simvastatin, terbinafine, terfenadine, tramadinone, valproic acid, zolpidem, or **pharmaceutically** acceptable salts of any of the abovementioned drugs.

DETD [0047] Suitable surface stabilizers can preferably be selected from known organic and inorganic **pharmaceutical** excipients. Such excipients include various polymers, low molecular weight oligomers, natural products, and surfactants. Preferred surface stabilizers include nonionic and . . .

DETD . . . (ICI Specialty Chemicals)); polyethylene glycols (e.g., Carbowaxs 3550® and 934® (Union Carbide)), polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate,

carboxymethylcellulose calcium, **carboxymethylcellulose** sodium, **methylcellulose**, **hydroxymylcellulose**, **hydroxypropylcellulose**, hydroxypropylmethyl-**cellulose** phthalate, noncrystalline **cellulose**, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol (PVA), **polyvinylpyrrolidone** (PVP), 4-(1,1,3,3-tetramethylbutyl)-phenol polymer with ethylene oxide and formaldehyde (also known as tyloxapol, superione, and triton), poloxamers (e.g., Pluronics F68® and . . .

DETD [0051] Most of these surface stabilizers are known **pharmaceutical**

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multilayer tablet may contain different active ingredient in each layer.
Multilayer tablets may optionally be coated with a controlled **release** polymer so as to provide additional controlled **release** properties.
DETD . . . coating may be applied to the tablets in any amount which is sufficient to give the desired degree of controlled **release**.
DETD [0039] In one embodiment a process for the manufacture of a controlled **release** composition comprises the steps of: (i) spray drying a nanoparticulate dispersion of a poorly soluble drug, optionally in the presence. . .
DETD [0074] In an another embodiment, a process for the manufacture of a controlled **release** composition comprises the steps of: (i) spray drying a nanoparticulate dispersion of a poorly soluble drug, optionally in the presence . . .
DETD [0077] The controlled **release** nanoparticulate formulations of the invention can be in the form of tablets for oral administration. Preparation of such tablets can be achieved by conventional means or molding techniques known in the art. The tablets of the invention may take any appropriate shape, such as. . .
DETD . . . techniques known to one of ordinary skill in the art are described in, for example, the 18th edition of Remington's **Pharmaceutical** Sciences, Chapter 89, pp. 1633-1658 (Mack Publishing Company, 1990), which is specifically incorporated by reference. In the simplest procedure, the. . .
DETD C. ADMINISTRATION OF CONTROLLED **RELEASE** NANOPARTICULATE COMPOSITIONS OR DOSAGE FORMS
DETD . . . method of treating a mammal, including a human, requiring extended administration of a drug or other agent. The administered controlled **release** nanoparticulate composition **releases** an incorporated drug or other agent over a prolonged period of time providing a desired effect for a period from.
DETD [0087] The purpose of this experiment was to demonstrate a reasonable amount of controlled **release** with a nanoparticulate drug formulation.
DETD [0088] 29% w/w spray-dried nanoparticulate naproxen intermediate (SDI) containing 97% w/w naproxen sodium and 3% w/w **polyvinylpyrrolidone** (PVP) as a surface stabilizer (sieve #20)), 30% w/w Klucel® EFC polymer (sieve #40), 40% w/w lactose (sieve #316 fast-fish, sieve #40), and 1% w/w magnesium stearate (Spectrum, sieve #40) were combined as free powders and **released** nanoparticulate formulation tablet to be tested.
DETD Testing For Controlled **Release**
DETD . . . Packard Diode Array Spectrophotometer 8452A and the Hewlett Packard Flow Control devices model 89092A) was used in testing for controlled **release**. The temperature (37° C.) and agitation of this instrument simulates the body system as it attempts to dissolve the
drug.
DETD . . . in dissolution of the tablets within a range of 40-50 min. Such
a time period is not suitable for controlled **release** applications.
DETD [0094] The purpose of this experiment was to demonstrate controlled **release** with a nanoparticulate drug formulation.
DETD [0097] To improve the controlled **release** characteristics of the formed tablets, (i) the weight of the tablet was increased from 500 to 750 mg, (ii) the. . .
DETD [0099] Following testing with the Distek Dissolution System, the results
demonstrated a steady controlled **release** of drug over a three hour time period, as shown in FIG. 3.
DETD [0100] The purpose of this experiment was to determine the effects of the hardness of a tablet on controlled **release** of the nanoparticulate agent.
DETD [0102] The results shown in FIG. 2 demonstrate that as the hardness of a
tablet increases, the controlled **release** characteristics of the tablet also steadily increase. Tablets having a hardness of about 15 kP, . . .
and 35 kP **released** naproxen for about 65 min., 140 min., and 240 min., respectively, showing a direct correlation between tablet hardness and increased controlled **release** of the administered agent.
DETD [0103] The purpose of this experiment was to compare the controlled **release** characteristics of two different rate-controlling polymers: Klucel® EFC and Shinetsu® L-HPC.
DETD . . . of 35 kP. The results, shown in FIG. 7, demonstrate that the tablet with 20% Klucel® as the polymer completely **released** within three to four hours, and the tablet with 20% Shinetsu® L-HPC as the polymer allowed the tablet to dissolve. . . .
DETD [0106] The purpose of this experiment was to compare the controlled **release** characteristics of different grades of Methocel® (hydroxypropyl methyl **cellulose** (HPMC) used as the rate-controlling polymer: (1) Methocel® K4M, (1) Methocel® K4M, (1) Methocel® K15M, (1v) Methocel® K100LV, (v) Methocel®. . .
DETD . . . kP. Each of the Methocel® grades tested in the Distek Dissolution system, was found to exert some extent of controlled **release** on the nanoparticulate formulation, as shown in FIG. 4. Methocel® grades K4M, K15 M, and K100M gave an extreme amount of controlled **release** (40-50% in 12 hours), Methocel® grade K4M dissolved in only about three hours, and Methocel® grades K100LV and K10M gave a **release** over about 12 to about 14 hours.
DETD [0109] The purpose of this example was to determine the effect of adding
hydrogenated vegetable oil (Lubritab®) to controlled **release** of a nanoparticulate agent.
DETD . . . As shown in FIG. 5, the addition of Lubritab® to a nanoparticulate formulation allow for an increase in controlled **release** of the administered agent. While the composition containing 0% Lubritab® was completely **released** at about 60 min., the composition containing 20% Lubritab® was **released** over about 175 min.
DETD [0112] The purpose of this example was to compare the controlled **release** properties of a composition of a spray-dried nanoparticulate formulation mixed with a rate-controlling polymer and a powder composition of unmilled.
DETD . . . in FIG. 6, the composition of raw drug and surface stabilizer blended with a rate-controlling polymer had a more prolonged **release** as compared to the composition of the spray-dried nanoparticulate formulation mixed with a rate-controlling polymer. The results indicate

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that complete **release** of the composition of raw drug and stabilizer blended with a rate-controlling polymer occurred after about 10 hours, while complete **release** of the spray-dried nanoparticulate formulation mixed with a rate-controlling polymer was expected to occur after about 13 to about 14 hours (complete **release** of the latter composition had not occurred after 12 hours, when the results were analyzed).
DETD [0113] The purpose of this example was to determine the effect of rate-controlling polymer concentration on the controlled **release** characterization of nanoparticulate formulations.
DETD [0116] The first test determined the controlled **release** characteristics of a nanoparticulate formulation comprising 5% Methocel® K100LV, and the second test determined the controlled **release** characteristics of a nanoparticulate formulation comprising 10% Methocel® K100LV. Controlled **release** characteristics of a nanoparticulate formulation comprising 20% Methocel® K100LV were obtained in Example 9 (FIG. 6) and are repeated here.
DETD . . . hardness and varying rate-controlling polymer concentrations, the tablet having the greatest rate-controlling polymer concentration will have the most prolonged **release** of the materials. The tablet having a 5% polymer concentration completely **released** after about 50 min.; the tablet having a 10% polymer concentration completely **released** after about 310 min., and the tablet having a 20% polymer concentration completely **released** after about 650 min. Thus, increased polymer concentration in the nanoparticulate formulation is directly correlated with prolonged **release** of the administered agent.
DETD [0119] The purpose of this example was to determine the effect of wet granulation on controlled **release** of nanoparticulate formulations
DETD . . . for both rate-controlling polymers, Klucel® EFC and Methocel® E5PRC, the tablets formed from wet granulation showed a much more controlled **release** than the normal dry mixture. The prolonged controlled **release** is likely due to the strength of the granules formed by the wet granulation technique. This binding is stronger than the binding of the materials by direct compression. Thus, wet granulation improves controlled **release**.
DETD [0122] The purpose of this example was to prepare a controlled **release** formulation of glipizide. Glipizide, also known as 1-cyclohexyl-3-[p-[2(5-methylpyrazine-carbouyamido)ethyl]-phenyl]-sulfonyl-urea, is an oral hypoglycemic.
DETD [0126] The results, shown in FIG. 9, indicate a steady **release** of drug over a time period of just under 18 hours (i.e., about 950 minutes).
DETD [0128] The purpose of this example was to prepare an uncoated controlled
release tablet formulation containing nanoparticulate nifedipine.
DETD . . . A colloidal dispersion of nifedipine in water was prepared. The
dispersion contained 30% (w/w) of the drug and 2% hydroxypropyl **cellulose**. Particle size analysis, performed using a Malvern Mastersizer S2.14 (Malvern Instruments Ltd., Malvern, Worcestershire, UK) recorded by a wet method. . . .
DETD . . . is given in Table 4.
TABLE 3

Blend formulation for Example 11
Ingredient Amount
Spray dried nifedipine 17.92
Avicel PH102 30.01

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Pharmacoat DC1 30.01
Methocel K 15M 20.00
Colloidal silicon dioxide 1.20
Magnesium stearate 0.86
DETD [0133]
TABLE 4

Dissolution data for uncoated nifedipine tablets prepared according to Example 11
Time (hr) % Active **Released**
1.0 17.8
2.0 24.9
4.0 37.3
6.0 49.1
8.0 61.5
10.0 71.5
22.0 108.8
DETD [0134] The purpose of this example was to prepare a coated controlled **release** tablet formulation containing nanoparticulate nifedipine.
DETD . . . is given in Table 7.
TABLE 7

Dissolution data for coated nifedipine tablets prepared according to Example 12
Time (hr) % Active **Released**
1.0 4.3
2.0 11.5
4.0 24.0
6.0 38.0
8.0 58.3
10.0 66.4
23.0 99.6
DETD [0138] FIG. 10 shows the mean in vivo plasma profiles in nine fasted human volunteers for (1) nifedipine containing controlled **release** matrix tablets coated with a controlled **release** coating according to the present invention as described in Example 12; and (2) a control composition. The study had a fully randomized, fully crossed over, single dose administration design. From the figure it can be seen that a
controlled **release** composition prepared according to Example 12 shows a high level of availability and shows good controlled **release** characteristics over a 24 hour period.
DETD [0139] The purpose of this example was to prepare an uncoated controlled
release tablet formulation containing nanoparticulate glipizide.
DETD . . . A colloidal dispersion of glipizide in water was prepared. The dispersion contained 30% (w/w) of the drug and 3% hydroxypropyl **cellulose**. Particle size analysis, performed using a Malvern Mastersizer S2.14, recorded by a wet method using a 150 ml flow through. . .
DETD . . . Table 8.
TABLE 8

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Composition prior to spray drying for Example 13

Ingredient	Amount (% by wt.)
Glipizide dispersion	10
Hydroxypropyl **cellulose**	3
Mannitol	15
Purified water	72

DETD . . . is given in Table 11.
TABLE 11

Dissolution data for uncoated glipizide tablets
prepared according to Example 13

Time (hr)	% Active **Released**
1.0	9.0
2.0	17.9
4.0	35.1
6.0	51.6
8.0	65.2
10.0	79.5
12.0	95.6

DETD [0145] The purpose of this example was to prepare delayed **release** nanoparticulate nifedipine capsules.
DETD [0146] A colloidal dispersion of nifedipine in water was prepared. The dispersion contained 10% w/w Nifedipine, 3% **hydroxypropylcellulose**, and 0.1% Poelxan Lauryl Sulphate in water. Particle size analysis, performed using a Malvern Mastersizer S2.14, recorded by a wet. . . .
DETD . . . given in Table 16.
TABLE 16

Dissolution data for Nifedipine 10 mg capsules
prepared according to Example 14

Time (hr)	% Active **Released**
0.25	3.99
0.5	4.60
0.75	21.10
1.0	93.07
1.5	100.39
2.0	100.79

DETD [0153] The purpose of this example was to prepare a control for delayed **release** nanoparticulate nifedipine capsules. The control does not contain a nanoparticulate composition.
DETD . . . given in Table 21.
TABLE 21

Dissolution data for Nifedipine 10 mg capsules
prepared according to Example 15

Time (hr)	% Active **Released**
0.25	8.83
0.5	32.50
0.75	77.88
1.0	85.26
1.5	91.90
2.0	94.46

DETD [0159] FIG. 11 shows the mean in-vivo plasma profiles of nifedipine in ten fasted human volunteers for (1) a controlled **release** composition manufactured according to the present invention as described in Example 14 (nifedipine 10 mg capsules (Dr,99 ex 500 nm); . . . single dose, fully randomized, fully crossed over, oral administration design. From the figure it can be seen that the controlled **release** composition manufactured according to the present invention shows an initial lag time followed by a rapid and high level of . . .
DETD [0160] It should be noted that the controlled **release** composition manufactured in accordance with the invention showed a relative bioavailability of 1.45 (i.e., 45% enhanced bioavailability as compared with.
CLM What is claimed is:
. . . 1. A controlled **release** nanoparticulate composition comprising: (a) a poorly soluble agent to be administered having an effective average particle size of less than . . . 1000 nm; (b) at least one surface stabilizer associated with the surface of the agent, and (c) at least one **pharmaceutically** acceptable rate-controlling polymer, wherein the composition provides controlled **release** of the agent for a time period ranging from about 1 to about 24 hours or longer.

CLM What is claimed is:
. . . added to the agent, surface stabilizer, and polymer to form granules prior to forming the solid dose of the controlled **release** formulation.

CLM What is claimed is:
. . . rate-controlling polymer is selected from the group consisting of gum

arabic, agar, guar gum, cereal gums, dextran, casein, gelatin, pectin, **carrageenan**, waxes, **shellac**, hydrogenated vegetable oils, **polyvinylpyrrolidone**, hydroxypropyl **cellulose** (HPC), hydroxyethyl **cellulose** (HEC), hydroxypropyl methyl **cellulose** (HPMC), sodium **carboxymethylcellulose** (CMC), polyethylene) oxide, silky **cellulose**, ethyl **cellulose**, methyl **cellulose**, microcrystalline **cellulose**, hydrophilic **cellulose** derivatives, polyethylene glycol, **polyvinylpyrrolidone**, **cellulose** acetate, **cellulose** acetate butyrate, **cellulose** acetate phthalate, **cellulose** acetate trimellitate, **polyvinyl** acetate phthalate, hydroxypropylmethyl **cellulose** phthalate, hydroxypropylmethyl **cellulose** acetate succinate, **polyvinyl** acetaldiethylamino acetate, poly(alkylmethacrylate), poly(vinyl acetate), polymers derived from acrylic or methacrylic acid and their respective esters, and copolymers derived from.

CLM What is claimed is:
. . . 14. A dosage form comprising a controlled **release** nanoparticulate composition according to claim 1, wherein the dosage form is in tablet form or in multiparticulate form.

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CLM What is claimed is:
. . . 14, wherein the agent, the rate controlling polymer and at least one auxiliary excipient are compressed to form a controlled **release** matrix tablet.

CLM What is claimed is:
. . . 17. The dosage form of claim 16, wherein the controlled **release** matrix is coated with a rate controlling polymer.

CLM What is claimed is:
. . . 29. The dosage form according to claim 14 wherein the tablet further comprises an osmagent added to the controlled **release** composition to form an admixture and a semi-permeable membrane; the semi-permeable membrane surrounding the admixture and being permeable to aqueous media,

but impermeable to the poorly soluble drug compound or **pharmaceutically** acceptable salt thereof and the semi-permeable membrane defining an orifice therein.

CLM What is claimed is:
. . . 30. A method of preparing a solid dose controlled **release** nanoparticulate formulation comprising: (a) combining a nanoparticulate

composition of an agent to be administered and at least one surface stabilizer; . . . and (b) forming a solid dose of the mixture from step (a), wherein the solid dose formulation has a controlled **release** of the agent following administration for a time period ranging from about 2 to about 24 hours or longer.

CLM What is claimed is:
. . . 35. A method of treating a mammal comprising administering to the mammal an effective amount of a solid dose controlled **release** nanoparticulate formulation wherein: (a) the formulation comprises nanoparticulate agent particles to be administered and at least one surface stabilizer associated . . . of less than about 1000 nm and at least one suitable rate-controlling polymer; and (b) the formulation has a controlled **release** of the agent following administration for a time period ranging from about 2 to about 24 hours or longer.

L57 ANSWER 40 OF 79 USPATFULL on STN

ACCESSION NUMBER: 2002:17267 USPATFULL
TITLE: Laundry detergents and cleaning products
INVENTOR(S): Schmiedel, Peter, Duesseldorf, GERMANY, FEDERAL REPUBLIC OF
Jekel, Nazes, Duesseldorf, GERMANY, FEDERAL REPUBLIC OF
Gassenmeier, Thomas Otto, Duesseldorf, GERMANY, FEDERAL
REPUBLIC OF
Von Rybinski, Wolfgang, Duesseldorf, GERMANY, FEDERAL REPUBLIC OF
Kessler, Arnd, Leverkusen, GERMANY, FEDERAL REPUBLIC OF
Hitsch, Christian, Duesseldorf, GERMANY, FEDERAL REPUBLIC OF
Bayersdoerfer, Rolf, Landau, GERMANY, FEDERAL REPUBLIC OF
Richter, Bernd, Leichlingen, GERMANY, FEDERAL REPUBLIC OF
Sunder, Matthias, Duesseldorf, GERMANY, FEDERAL REPUBLIC OF
Holderbaum, Thomas, Monheim, GERMANY, FEDERAL REPUBLIC OF

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20020010123	A1	20020124
APPLICATION INFO.:	US 2000-731395	A1	20001204 (9) <--

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1999-19958471	19991204 <--
	DE 2000-10019936	20000420 <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Glenn E.J. Murphy, Henkel Corporation, Patent Law Dept., 2500 Renaissance Blvd., Suite 200, Gulph Mills, PA, 19406
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
LINE COUNT: 1515
AB Claimed are laundry detergents and cleaning products which comprise customary ingredients and, characteristically, further comprise an active substances preparation which has been compounded with an LCST substance. By means of compounding with an LCST substance it is possible

to incorporate active substances which, in a washing or cleaning process

which passes through one or more temperature stages, are **released** only after a heat treatment, e.g. only in a rinse cycle

AB . . . . to incorporate active substances which, in a washing or cleaning process which passes through one or more temperature stages, are **released** only after a heat treatment, e.g., only in a rinse cycle
SUMM [0002] The controlled **release** of active substances has a part to play wherever the active substance is intended to develop its activity not

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immediately.
SUMM [0023] In the **pharmaceutical** sector, the different dissolution behaviour of polymers in the acidic and alkaline medium, i.e., as in the stomach and in . . . least part of the material being present in encapsulated form during a heat treatment in an aqueous environment and being **released** after cooling following this heat treatment. This material is coated with a layer comprising a hydrophobic film-forming material and with a . . .
SUMM . . . comprises an active substance which, in a washing or cleaning process which passes through one or more temperature stages, is **released** only after a heat treatment, e.g., only in a rinse cycle.
SUMM [0028] It has surprisingly been found that active substances in washing and cleaning processes can be **released** specifically only in a rinse cycle if these active substances are incorporated into the **compositions** are compounded with an . . . textile detergents and also textile aftertreatment compositions, these compositions being able to comprise exclusively active substances which are to be **released** only in a process stage following the actual cleaning or laundering, and which are therefore not . . . available during the actual . . .
SUMM . . . carbonates, silicates, phosphates, and also synthetic polymers, such as polyethylene glycols, for example, especially solid polyethyne . . . glycols, polycarboxylates, crosslinked polycarboxylates, **polyvinyl** alcohols with different degrees of hydrolysis and molecular weight, or **polyvinylpyrrolidone**, **polyvinyl** acetate, and organic oligocarboxylic acids which are solid at room temperature. The LCST polymers used may also be suitable carrier. . . .
SUMM . . . detergent or cleaning product may be used with particular advantage in machine processes where the active substance is to be **released** in a wash cycle following the washing step. Examples are the machine laundering of textiles and the machine washing of . . . unchanged following a heat treatment in a liquid medium, e.g., following
SUMM the main wash cycle, and the active substance is **released** only after cooling following the heat treatment, i.e., in the rinse cycle.
SUMM [0029] In accordance with the invention, the active substance intended for delayed **release** is compounded with an LCST substance. LCST substances are substances which have a water solubility at low temperatures that at . . . C., in particular between 30° C. and 50° C. The LCST substances are preferably selected from alkylated and/or hydroxyalkylated polysaccharides, **cellulose** ethers, polyisopropylacrylamide, copolymers of polyisopropylacrylamide, and blends of these substances.
SUMM [0021] Examples of alkylated and/or hydroxyalkylated polysaccharides are

methylhydroxypropylmethylcellulose (MHPC),
ethyl hydroxyethyl **cellulose** (EHEC), **hydroxypropylcellulose** (HPC), **methylcellulose** (MC), **ethylhydroxyethylcellulose** (EHEC), **carboxymethylmethylcellulose** (CMMC), **hydroxybutylcellulose** (HBC), **hydroxybutylmethylcellulose** (HBMC), **hydroxyethylcellulose**

L57 ANSWER 40 OF 79 USPATFULL on STN (Continued)
. . . with an LCST substance and may be incorporated into the composition of the invention. In the wash process, they are **released** in a rinse cycle following the main wash cycle.
SUMM [0039] Bleaches may also be compounds which **release** chlorine or bromine. Among the activators, the acetonitrile quats and trialkylamine examples include heterocyclic N-bromoamides and N-chloramides, examples . . . being trichloroisocyanuric acid, tribromoisocyanuric acid, dibromoisocyanuric acid and dichloroisocyanuric acid (DICA) and/or. . . .
SUMM . . . to apply the fragrances to carriers, which strengthen the adherence of the perfume to the laundry and, by slowing the **release** of fragrance, provide for long-lasting fragrance of the treated Materials . . . which have become established as such carriers are, for example, . . . to be coated with further auxiliaries. Compounding the fragrances with an LCST substance is also possible, so that they are **released** only in the rinse cycle, which results in a fragrance sensation when the machine . . . is opened.
SUMM [0039] As further active substances which may be incorporated in compositions of the invention or else may be **released** at early as in the main wash cycle, the compositions used as machine dishwashing compositions may comprise corrosion inhibitors. The . . .
SUMM [0039] Laundry detergent and cleaning products used for textile laundering may include cationic surfactants as active substances which may be **released** only in the rinse cycle. . . .
SUMM [0108] The active substances in the phase(s) A are preferably not **released** until a process stage following the heat treatment, preferably in the rinse cycle, and the active substances of phases B are preferably . . . **released** before or during the heat treatment, e.g., in the main wash cycle. . . .
SUMM . . . the composition of the invention, a fraction of the active substances is incorporated in such a way that it is **released** not at all or only to a minor extent in the main wash cycle (and also in optional prewash cycles). . . . machine and to the detergent solution. This ensures that the active substance is present in the rinse cycle and is **released** only in this cycle, where it performs the desired action. Examples of dishwashing compositions that are preferred in the context. . . . Interesting variations may also be realized in this way by providing the active substance, if it is to be **released** in the rinse cycle, of a machine dishwashing process, in the form of a stylized glass, in order to undercoate. . . .
DETD . . . beginning of the rinse cycle. It breaks down in the first few minutes of the rinse cycle and, as desired, **releases** the rinse aid surfactant . . . the beginning of the rinse cycle, but then breaks down during the first few minutes of the rinse cycle, and **releases** the rinse aid.
DETD . . . of the rinse cycle, but then breaks down in the first few minutes of the said cycle and, as desired, **releases** the rinse aid.
DETD [0141] 35% by weight of **polyvinyl** alcohol (Clariant PVAL Mowiol® 4-88), 15% **polyvinyl** acetate (Sue PVAc SLP 3213) and 50% Polyergent® SLF 18B45 were mixed with one another at a temperature of 70° C. . . .
DETD [0143] 45% by weight of **polyvinyl** alcohol (Kroll® 05/140), 15% of PEG 6000 and 40% of Polyergent® SLF 18B45 were mixed with one

L57 ANSWER 40 OF 79 USPATFULL on STN (Continued)
(HEC), **hydroxyethylcarboxymethylcellulose** (HECMC), **hydroxyethylethylcellulose** (HEEC), **hydroxypropylcellulose** (HPC), **hydroxypropylcarboxymethylcellulose** (HPCMC), **hydroxyethylmethylcellulose** (HEMC), **methylhydroxyethylcellulose** (MEHEC), **methylcellulose** (MC), and **propylcellulose** (PC) and mixtures thereof, preference being given to **carboxymethylcellulose**, **methylcellulose** and **methylhydroxyethylcellulose** and **methylhydroxypropylcellulose** and also to the alkali metal salts of CMC and the slightly ethoxylated MCs or mixtures of the above.
SUMM [0022] Further examples of LCST substances are **cellulose** ethers and also mixtures of **cellulose** ethers with **carboxymethylcellulose** (CMC). Further polymers which exhibit a lower critical separation temperature in water and which are likewise suitable as polymers for . . . or copolymers thereof, such as ethylene oxide/propylene oxide copolymers and graft copolymers of alkylene oxides and acrylic acid, polymethacrylic acid, **polyvinyl** alcohol and copolymers thereof, **polyvinyl** methyl ether, certain proteins such as polyvalinlysyl, a repeating unit in the natural protein elastin, and certain alginates. Mixtures of . . . of the LCST substance or which has a melting point above this temperature or a retarded solubility, i.e., can be **released** above the lower separation temperature of the LCST coat. The purpose of this coat is to protect the mixture of . . .
SUMM [0023] Preferred substances which may be applied as a further coat are hydrophilic polymers, such as **polyvinyl** alcohols, polyethylene glycols, **polyvinylpyrrolidone**, water-soluble polysaccharides, water-soluble polyurethanes, and the gums, gum arabic, alginates, chitosan, **carrageenan**, polyacrylates and copolymers thereof. **Shellac** as well, such as Schellack-Service-GmbH (Hildebad GmbH), for example, may be used as further substances. . . .
SUMM . . . polymer used in accordance with the invention or which are soluble above this temperature. Suitable polymers are room-temperature-solid polyethylene glycols, **polyvinyl** alcohols, polyacrylic acid and derivatives thereof. Gelatin has also proven suitable. . . .
SUMM . . . the present invention it is possible first to coat the active substances with a coat of a water-soluble polymer, e.g. **polyvinyl** alcohol, to which the LCST substance is applied subsequently. . . . coat for the active substance, which is intended to prevent the diffusive penetration of water and thus premature dissolution and **release** of said substance. It is also possible to coat the solid carrier that . . . the application of further coats below the LCST substance. . . .
SUMM [0036] The active substance used which is intended for retarded **release** may be processed, i.e., compounded, in a manner known per se with the LCST substance and/or the further material. Where. . . is a further option. In the case of the spraying method, suitable processes are all those which are established in **pharmacy** and food technology for the production of coated tablets, capsules and particles. The polymer suspension or solution is applied to . . .
SUMM . . . essential advantage of the laundry detergent or cleaning product of the invention is that the active substances are to be **released** in a process stage following a heating step, i.e., in the rinse cycle, need not be added separately. The majority. . . .

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another at a . . .
DETD . . . coating was applied to the compacts of example 9 by immersing them in an alcoholic solution of 5% by weight of **polyvinyl** alcohol ether, BASF). Subsequently, a further coating of wax or shellac was applied.
DETD [0180] In a fluidized-bed apparatus, the granules were coated with 0.77% of **polyvinyl** alcohol Erkol M25/140. They were subsequently compressed on a tableting press to form 0.9 g compacts.
CLM What is claimed is:
. . . carbonates, especially alkali metal carbonates, hydrogen carbonates, sulfates, phosphates, and also synthetic polymers, such as polyethylene glycols, polycarboxylates, crosslinked polycarboxylates, **polyvinyl** alcohols with different degrees of hydrolysis, or **polyvinyl** acetate, and organic oligocarboxylic acids which are solid at room temperature.
CLM What is claimed is:
. . . unchanged following a heat treatment in a liquid medium in the main wash cycle and, following a temperature reduction, is **released** subsequent to the heat treatment.
CLM What is claimed is:
. . . detergent or cleaning product as claimed in any of claims 1 to 6, wherein the LCST polymers is selected from **cellulose** derivatives, monoor di-N-alkylated acrylamides, copolymers of mono- or di-N-substituted acrylamides with acrylamides and/or acrylates and/or acrylic acids, **polyvinyl** alcohol and copolymers thereof, such as **polyvinyl** alcohol-vinyl acetate copolymers, **polyvinyl** methyl ethers, **polyvinyloxazolines**, polyvinylmethyloxazolidine and copolymers, polyisopropylacrylamide, polyamino acids and/or proteins.
CLM What is claimed is:
. 8. The laundry detergent or cleaning product as claimed in claim 7, wherein the LCST polymer is selected from **cellulose** ethers, polyisopropylacrylamide, copolymers of polyisopropylacrylamide, and blends of these substances.
CLM What is claimed is:
. . . detergent or cleaning product as claimed in claim 11, wherein the further substance is selected from hydrophilic polymers, such as **polyvinyl** alcohols, polyethylene glycols, water-soluble polysaccharides, water-soluble polyurethanes, xanthan, gear gum, alginates, chitosan, **carrageenan**, polyacrylates, **shellac**, polyacrylates and copolymers thereof and also any desired mixtures of the above.
CLM What is claimed is:
. 15. The laundry detergent or cleaning product as claimed in claim 14, wherein the layer of water-soluble polymer comprises **polyvinyl** alcohol.
CLM What is claimed is:
. . . The laundry detergent or cleaning product as claimed in claim 21, wherein the phase(s) A comprise(s) active substances which are **released** in a cycle after the actual dishwashing, preferably in the rinse cycle.

L57 ANSWER 41 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2002:13960 USPATFULL
TITLE: FLUIDIZED BED MATRIX GRANULE
INVENTOR(S): BECKER, NATHANIEL T., BURLINGAME, CA, UNITED STATES
CHRISTENSEN, ROBERT I., JR., PINOLE, CA, UNITED STATES
GROS, ERNST B., KANTVIK, FINLAND

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20020002835	A1	20020103
	US 6423517	B2	20020723
APPLICATION INFO.:	US 1999-215096	A1	19981218 (9) <--
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1997-995490, filed on 20 Dec 1997, ABANDONED		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	KIRKPATRICK & ANDERSON, GENENCOR INTERNATIONAL INC, 925 PAGE MILL ROAD, PALO ALTO, CA, 943041013		
NUMBER OF CLAIMS:	27		
EXEMPLARY CLAIM:	1		
LINE COUNT:	560		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Granules that include a protein core are described. The protein core includes a protein matrix which includes a protein mixed together with a

salt. The protein matrix is layered over a seed particle. The protein can be an enzyme or a therapeutic protein such as a hormone. Methods of making the granules are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM6 [0002] Proteins such as **pharmaceutically** important proteins like hormones and industrially important proteins like enzymes are becoming more widely used. Enzymes, for example, are used . . .

SUM6 . . . U.S. Pat. No. 4,106,991 describes an improved formulation of enzyme granules by including within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-40% w/w based on the dry weight of the whole composition. In addition, this patent . . .

SUM6 . . . diatomaceous earth or sodium nitrate crystals. The film forming

material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.

SUM6 . . . and improved stability formulations. Accomplishing all these desired characteristics simultaneously is a particularly challenging task since, for example, many delayed **release** or low-dust agents such as fibrous **cellulose** or waxy size polymers leave behind insoluble residues.

SUM6 . . . There can be one or more layers between the seed particle and the matrix, for example, a coating such as **polyvinyl** alcohol.

SUM6 [0028] Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as enzymes.

SUM6 . . . natural polymers such as starch, modified starch, carrageenan,

L57 ANSWER 41 OF 79 USPATFULL on STN (Continued)
gum arabic and guar gum and synthetic polymers such as polyethylene oxide, **polyvinyl** pyrrolidone, polyethylene glycol and polyethylene oxide/polypropylene oxide.

SUM6 [0034] Suitable coatings include water soluble or water dispersible film-forming polymers such as **polyvinyl** alcohol [PVA], **polyvinyl** pyrrolidone [PVP], **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, gum arabic, xanthan, **carrageenan**, chitosan, latex polymers, and enteric **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.

SUM6 . . . Preferably, the outer coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, **polyvinyl** pyrrolidone-vinyl PVP-PVA copolymer.

DETD . . . osmotically coated with 2116 grams of an aqueous solution containing 131 grams (6.2% w/w) titanium dioxide, 53 grams (2.5% w/w) **methylcellulose** marketed under the trade name Methocel A-15LV (Dow Chemical Corp.), 53 grams (2.5% w/w) of maltodextrin M150 (DE-15 from Grain . . .

CLM What is claimed is:
. . . wherein the binder is selected from the group consisting of starch, modified starch, carrageenan, gum arabic, guar gum, polyethylene oxide, **polyvinyl** pyrrolidone, and polyethylene glycol.

CLM What is claimed is:
9. The granule of claim 6, wherein the coating is selected from the group consisting of **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan and carrageenan.

CLM What is claimed is:
. . . wherein the binder is selected from the group consisting of starch, modified starch, carrageenan, gum arabic, guar gum, polyethylene oxide, **polyvinyl** pyrrolidone, and polyethylene glycol.

CLM What is claimed is:
18. The granule of claim 15, wherein the coating is selected from the group consisting of **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan and carrageenan.

CLM What is claimed is:
. . . wherein the binder is selected from the group consisting of starch, modified starch, carrageenan, gum arabic, guar gum, polyethylene oxide, **polyvinyl** pyrrolidone, and polyethylene glycol.

CLM What is claimed is:
27. The method of claim 24, wherein the coating is selected from the

L57 ANSWER 42 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2001:238056 USPATFULL
TITLE: Matrix granule
INVENTOR(S): Becker, Nathaniel T., Burlingame, CA, United States
Green, Thomas S., Montara, CA, United States
Christensen, Robert I., JR., Pinole, CA, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20010054177	A1	20011227
APPLICATION INFO.:	US 2001-886244	A1	20010620 (9) <--
RELATED APPLN. INFO.:	Division of Ser. No. US 1998-215095, filed on 18 Dec 1998, PENDING Continuation-in-part of Ser. No. US 1997-995490, filed on 20 Dec 1997, ABANDONED		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-1058749	19981027 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Genencor International, Inc., 925 Page Mill Road, Palo Alto, CA, 94304-1013	
NUMBER OF CLAIMS:	56	
EXEMPLARY CLAIM:	1	
LINE COUNT:	1037	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Granules that include a protein core are described. The protein core includes a protein matrix which includes a protein mixed together with a

combination of a sugar or sugar alcohol and a structuring agent such as a polysaccharide or a polypeptide. The protein matrix can be layered over a seed particle or the protein core can be homogenous. The protein can be an enzyme or a therapeutic protein such as a hormone. Also described are methods for making the granules.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM6 [0002] Proteins such as **pharmaceutically** important proteins like hormones and industrially important proteins like enzymes are becoming more widely used. Enzymes are used as several . . .

SUM6 . . . U.S. Pat. No. 4,106,991 describes an improved formulation of enzyme granules by including within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-40% w/w based on the dry weight of the whole composition. In addition, this patent . . .

SUM6 . . . diatomaceous earth or sodium nitrate crystals. The film forming

material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.

SUM6 . . . perborate or sodium percarbonate. Accomplishing all these desired characteristics simultaneously is a particularly challenging task since, for example, many delayed **release** or low-dust agents such as fibrous **cellulose** or kaolin leave behind insoluble residues.

SUM6 . . . between the seed particle and the matrix or the matrix and the barrier layer, for example, a coating such as **polyvinyl** alcohol (PVA).

SUM6 [0075] Preferred structuring agents include starch, modified starch, carrageenan, **cellulose**, modified **cellulose**, gum arabic, guar gum, acacia gum, xanthan gum, locust bean gum, chitosan, gelatin, collagen,

L57 ANSWER 42 OF 79 USPATFULL on STN (Continued)
casein, polyaspartic acid and polyglutamic acid.
SUMM [0036] Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as enzymes.
SUMM . . . more synthetic polymers or other excipients as known to those skilled in the art. Suitable synthetic polymers include polyethylene oxide, **polyvinyl** alcohol, **polyvinyl** pyrrolidone, polyethylene glycol and polyethylene oxide/polypropylene oxide.
SUMM [0042] Suitable coatings include water soluble or water dispersible film-forming polymers such as **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, gum arabic, xanthan, **carrageenan**, chitosan, latex polymers, and acrylic **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.
SUMM . . . Preferably, the outer coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVA-methylmethacrylate copolymer and PVP-PVA copolymer.
DETD . . . . . cosmetically coated with 2356 grams of an aqueous solution containing 146 grams (6.2% w/w) titanium dioxide, 118 grams (5% w/w) **methylcellulose** (Methocel A15-LV, Dow Chemical), 24 grams (1% w/w) of Neodol 23/6.5 (Shell Chemical Co.) and 39 grams (1.67% w/w) of . . . . . cosmetically coated with 2356 grams of an aqueous solution containing 146 grams (6.2% w/w) titanium dioxide, 118 grams (5% w/w) **methylcellulose**, 24 grams (1% w/w) of Neodol 23/6.5 and 39 grams (1.67% w/w) of polyethylene glycol at a MW of 600. . . .
DETD . . . . . cosmetically coated with 208.93 kg of an aqueous solution containing 12.97 kg (6.2% w/w) titanium dioxide, 10.39 kg (5% w/w) **methylcellulose**, 2.12 kg (1% w/w) of Neodol 23/6.5 and 7.57 kg (1.67% w/w) of polyethylene glycol at a MW of 600. . . .
DETD . . . . . cosmetically coated with 240.78 kg of an aqueous solution containing 14.97 kg (6.2% w/w) titanium dioxide, 6.84 kg (2.5% w/w) **methylcellulose**, 6.84 kg (2.5% w/w) hydroxypropyl methylcellulose 2910 (USP Grade from Grain Processing Corp., Muscatine, Iowa), 2.74 kg (1% w/w) of Neodol.
.
DETD [0082] Finally, a coating solution was prepared by dissolving or suspending 17.9 kg Nivasol 51-05 **polyvinyl** alcohol, 22.4 kg titanium dioxide, and 6.5 kg Neodol 23.5-87 nonionic surfactant in water to a net
DETD weight of 224.1. . . . . cosmetically coated with 92.6 kg of an aqueous solution containing 7.1 kg (6.2% w/w) titanium dioxide, 2.9 kg (2.5% w/w) **methylcellulose**, 2.9 kg (2.5%) Pursorte B790, 1.2kg (1.5% w/w) Neodol 23/6.5, and 2.3 kg (1.67% w/w) polyethylene glycol at a. . .
DETD [0093] Finally, a coating solution was prepared by adding 5.29 kg Methocel A-15 **methylcellulose** (Dow Chemical), 12.71 kg titanium dioxide (DuPont), 5.29 kg Pure Cote B-790 modified sraarch (Grain Processing Corp.), 2.12 kg Neodol. . .

L57 ANSWER 42 OF 79 USPATFULL on STN (Continued)
CLM What is claimed is:
. . . 2. The granule of claim 1, wherein the structuring agent is selected from the group consisting of starch, modified starch, **cellulose**, modified **cellulose**, carrageenan, gum arabic, acacia gum, xanthan gum, locust bean gum, and guar gum.
CLM What is claimed is:
. . . claim 1, further comprising a synthetic polymer, wherein the synthetic polymer is selected from the group consisting of polyethylene oxide, **polyvinyl** alcohol, **polyvinyl** pyrrolidone, polyethylene glycol and polyethylene oxide/polypropylene oxide.
CLM What is claimed is:
11. The granule of claim 8, wherein the coating is selected from the group consisting of **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan and carrageenan.
CLM What is claimed is:
. . . The granule of claim 13, wherein the structuring agent is selected from the group consisting of starch, modified starch, carrageenan, **cellulose**, modified **cellulose**, gum arabic, acacia gum, xanthan gum, locust bean gum, and guar gum.
CLM What is claimed is:
. . . claim 12, further comprising a synthetic polymer, wherein the synthetic polymer is selected from the group consisting of polyethylene oxide, **polyvinyl** alcohol, **polyvinyl** pyrrolidone, polyethylene glycol and polyethylene oxide/polypropylene oxide.
CLM What is claimed is:
22. The granule of claim 19, wherein the coating is selected from the group consisting of **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan and carrageenan.
CLM What is claimed is:
. . . The granule of claim 24, wherein the structuring agent is selected from the group consisting of starch, modified starch, carrageenan, **cellulose**, modified **cellulose**, gum arabic, acacia gum, xanthan gum, locust bean gum, and guar gum.
CLM What is claimed is:
. . . claim 23, further comprising a synthetic polymer, wherein the synthetic polymer is selected from the group consisting of polyethylene oxide, **polyvinyl** alcohol, **polyvinyl** pyrrolidone, polyethylene glycol and polyethylene oxide/polypropylene oxide.
CLM What is claimed is:
33. The granule of claim 30, wherein the coating is selected from the

L57 ANSWER 43 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2001:191098 USPATFULL
TITLE: Fluidized bed low density granule
INVENTOR(S): Boutin, Jean-Pierre, Rueil-Malmaison, FR, United States
Bonnet, Jacques, Le Pecq, FR, United States
PATENT ASSIGNEE(S): Genencor International, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6210027	B1	20010930	
	WO 2000029534		20000525	<--
APPLICATION INFO.:	US 2000-462431		20000107 (9)	<--
	WO 1999-US26910		19991112	<--
			20000107	PCT 371 date
			20000107	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-108417P	19981113 (60) <--
DOCUMENT TYPE:	UTILITY	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Dunston, Lorna M.	
LEGAL REPRESENTATIVE:	Genencor International	
NUMBER OF CLAIMS:	14	
EXEMPLARY CLAIM:	1	
LINE COUNT:	701	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A multi-layer enzyme granule for use in liquid detergents and cleaners is produced, comprising a seed or carrier particle; an outer coating; and, between the particle and the coating layer, a low-density filler and an enzyme, wherein the granule has a density of less than 1.4 g/cm.sup.3. Also disclosed are methods for making such enzyme-containing granules including using fluidized bed technology.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AI	19991112
	20000107 PCT 371 date
	20000107 PCT 102(e) date

SUMM The use of proteins such as **pharmaceutically** important proteins, e.g., hormones, and industrially important proteins, e.g., enzymes, has been rapidly growing in recent years. Today, for example,
SUMM U.S. Pat. No. 4,106,991 describes an improved formulation of enzyme granules by including within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-40% w/w based on the dry weight of the whole composition. In addition, this patent . . . . . distaneaceous earth or rodiun citrate crystals. The film forming
material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.
SUMM . . . . . in storage (e.g., greater than 50%). Moreover, an especially desirable granule would additionally disintegrate quickly in the wash liquor to **release** its enzyme activity. It is an advantage of the present invention to provide granules meeting such specifications.
SUMM . . . . . porous material. For example, the filler can be selected from one or more of the following: perlite, fumed silica, starch, **cellulose**

L57 ANSWER 43 OF 79 USPATFULL on STN (Continued)
fibers, DE, feather particles, zeolites, flour, fragments of milled plant-derived materials.
SUM36 Acceptable fillers include perlite, fumed silica, starch, **cellulose** fibers, DE, feather particles, zeolites, flour, fragments of milled plant-derived materials, and any mixture thereof. Particularly preferred
fillers are porous
SUM36 Acceptable fillers include starch, **cellulose** fibers, DE, feather particles, zeolites (such as used for molecular sieving), flour, milled plant derived fragments such as corn cobs, . . .
SUM36 Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as enzymes.
SUM36 Suitable synthetic polymers include polyethylene oxide, **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **polyvinyl** pyridine, polyethylene glycol and polyethylene oxide/polypropylene oxide.
SUM36 Suitable coatings include water soluble or water dispersible film-forming polymers such as **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, gum arabic, xanthan, **carrageenan**, chitosan, latex polymers, and enteric **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.
SUM36 . . . Preferably, the outer coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVA-methylmethacrylate copolymer and PVP-PVA copolymer and enteric co-polymers such as those sold under the. . . .
DETD . . . applied using 50 psi atomization pressure. To the resulting product, a solution of 117 g titanium dioxide, 94 g methyl **cellulose** (Methocel A1 5), 32 g polyethylene glycol (PEG 600) and 19 g surfactant (Neodol 23-6.5) was applied. The resulting product. . . .
DETD . . . applied using 50 psi atomization pressure. To the resulting product, a solution of 117 g titanium dioxide, 94 g methyl **cellulose** (Methocel A15), 32 g polyethylene glycol (PEG 600) and 19 g surfactant (Neodol 23-6.5) was applied. The resulting product weighed. . . .
DETD . . . g water was applied using 50 psi. To the resulting product, a solution of 128 g titanium dioxide, 102 g **polyvinyl** alcohol (Elvanol 51-05) and 26 g surfactant (Neodol 23-6.5) in 904 g water was applied. The resulting product weighed 1690. . . .
DETD . . . atomization air and 100C inlet air temperature. To the resulting product, a solution of 9.75 kg titanium dioxide, 7.8 kg **polyvinyl** alcohol (Elvanol 51-05) and 1.95 kg surfastant (Neodol 23-6.5) in 69.14 kg water was applied. The resulting product weighed 168.0.
CLM What is claimed is:
. . . of claim 1, wherein the low-density filler is a material selected from the group consisting of perlite, fumed silica, starch, **cellulose** fibers, zeolites, and borosilicate glass, fused glass, ceramic, and plastic hollowspheres.

L57 ANSWER 44 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2001:182558 USPATFULL
TITLE: Fluidized bed low density granule
INVENTOR(S): Dale, Douglas A., Fairfield, OH, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20010037717	A1	20011108
	US 6635611	B2	20031021
APPLICATION INFO.:	US 2001-846210	A1	20010525 (9) <--
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-462431, filed on 7 Jan 2000, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-108417P	19981113 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Spencer International, Inc., 925 Page Mill Road, Palo Alto, CA, 94304	
NUMBER OF CLAIMS:	29	
EXEMPLARY CLAIM:	1	
LINE COUNT:	754	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides low-density enzyme-carrying granules that
are low-dusting and/or storage-stable, and especially suitable for use in liquid detergents and cleaners, such as non-aqueous liquid laundry detergents. Preferred granules of the invention include a relatively high content of one or more low-density fillers, such as perlite or starch, to provide a desired product density. In one embodiment, the granules have a true density within a range of from about 1 to about 1.4
g/cm.sup.3. The granules are economically produced in commercial quantities using fluidized bed technology.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUM1 [0002] The use of proteins such as **pharmaceutically** important **proteins**, e.g., hormones, and industrially important proteins, e.g., enzymes, has been rapidly growing in recent years. Today, for example, .
SUM1 . . . U.S. Pat. No. 4,106,991 describes an improved formulation of enzyme granules by including within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-40% w/w based on the dry weight of the whole composition. In addition, this patent.
SUM1 . . . diatomaceous earth or sodium citrate crystals. The film forming
material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.
SUM1 . . . in storage (e.g., greater than 50%). Moreover, an especially desirable granule would additionally disintegrate quickly in the wash liquor to **release** its enzyme activity. It is an advantage of the present invention to provide granules meeting such specifications.
SUM1 . . . porous material. For example, the fillers can be selected from one or more of the following: perlite, fumed silica, starch, **cellulose** fibers, DE, feather particles, zeolites, flour, fragments of milled

L57 ANSWER 44 OF 79 USPATFULL on STN (Continued)
SUM1 [0047] Acceptable fillers include perlite, fumed silica, starch, **cellulose** fibers, DE, feather particles, zeolites, flour, fragments of milled plant-derived materials, and any mixture thereof. Particularly preferred fillers are porous.
SUM1 [0068] Acceptable fillers include starch, **cellulose** fibers, DE, feather particles, zeolites (such as used for **molecular** sieving), flour,
milled plant derived fragments such as corn cobs, . . .
SUM1 [0071] Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as enzymes.
SUM1 [0073] Suitable synthetic polymers include polyethylene oxide, **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **polyvinyl** pyridine, polyethylene glycol and polyethylene oxide/polypropylene oxide.
SUM1 [0077] Suitable coatings include water soluble or water dispersible film-forming polymers such as **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, gum arabic, xanthan, **carrageenan**, chitosan, latex polymers, and enteric **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.
SUM1 . . . Preferably, the outer coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVP-methylmethacrylate copolymer and PVP-PVA copolymer and enteric co-polymers such as those sold under the. . . .
DETD . . . applied using 50 psi atomization pressure. To the resulting product, a solution of 117 g titanium dioxide, 94 g methyl **cellulose** (Methocel A15), 32 g polyethylene glycol (PEG 600) and 19 g surfactant (Neodol 23-6.5) was applied. The resulting product weighed. . . .
DETD . . . applied using 50 psi atomization pressure. To the resulting product, a solution of 117 g titanium dioxide, 94 g methyl **cellulose** (Methocel A15), 32 g polyethylene glycol (PEG 600) and 19 g surfactant (Neodol 23-6.5) was applied. The resulting product weighed. . . .
DETD . . . g water was applied using 50 psi. To the resulting product, a solution of 128 g titanium dioxide, 102 g **polyvinyl** alcohol (Elvanol 51-05) and 26 g surfactant (Neodol 23-6.5) in 904 g water was applied. The resulting product weighed 1689. . . .
DETD . . . atomization air and 100C inlet air temperature. To the resulting product, a solution of 9.75 kg titanium dioxide, 7.8 kg **polyvinyl** alcohol (Elvanol 51-05) and 1.95 kg surfastant (Neodol 23-6.5) in 69.14 kg water was applied. The resulting product weighed 168.0. . . .
CLM What is claimed is:
. . . The granule of claim 19, wherein the filler is selected from the group
of consisting of perlite, fumed silica, starch, **cellulose** fibers, DE, feather particles, zeolites, flour, fragments of milled plant-derived materials, and any mixture thereof.

CLM What is claimed is:
. . . The granule of claim 19, wherein the filler is selected from the group of consisting of perlite, fumed silica, starch, **cellulose**

L57 ANSWER 44 OF 79 USPATFULL on STN (Continued)
fibers, DL, feather particles, zeolites, flour, fragments of milled plant-derived materials, and any mixture thereof.

L57 ANSWER 45 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2001:173179 USPATFULL
TITLE: Protective coating for food, method for producing same and products coated by same
INVENTOR(S): Nussinovitch, Amos, Petach Tikva, Israel
Hershko, Varda, Rehovot, Israel
Nahoumovitch, Naim D., Pyrisat Ono, Israel
PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Jerusalem, Israel (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6299915	B1	20011009
APPLICATION INFO.:	US 2000-521959		20000309 (9) <---
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 836402, now patented, Pat. No. US 6068867		

	NUMBER	DATE
PRIORITY INFORMATION:	IL 1995-111495	19951102 <---
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Corbin, Arthur L.	
LEGAL REPRESENTATIVE:	Browdy and Neimark	
NUMBER OF CLAIMS:	17	
EXEMPLARY CLAIM:	16	
NUMBER OF DRAWINGS:	4 Drawing Figure(s); 4 Drawing Page(s)	
LINE COUNT:	597	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a hydrocolloid protective coating for food and/or agricultural products comprising:

5-95% dried hydrocolloid gel;

0.2-90% of one or more natural compounds isolated from the surface of said product or a compound substantially equivalent thereto;

4-30% of water; and

optional additives.

The protective coating provides improved protection of the product, thereby extending its shelf-life. A method for producing the coating, and food and agricultural products protected by the coating are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM . . . as opticnally at least one antioxidant, a plant growth regulator and/or a chilling injury protectant. The polysaccharide polymer is preferably **carboxymethylcellulose**, but instead may be another hydrocolloid. Regardless, the polysaccharide polymer, even if a hydrocolloid, is not of the type which. . .

L57 ANSWER 45 OF 79 USPATFULL on STN (Continued)
DRWD . . . graph depicting the weight loss of garlic bulbs as a function of time in another embodiment of the invention--garlic bulbs **coated** by a F-**Carrageenan** with β-sitosterol (.quadrature.) Comparison to **coating** with F-**Carrageenan** without a further additive (.circle-solid.), to F-Carrageenan together with commercial wax (.circle-solid.) a nd to no coating (.smallcircle.) is also. . . .

DETD . . . weight loss of F-carrageenan treated bulbs was by 1.8% less than uncoated controls whereas weight loss of bulbs having a **coating** of F-**carrageenan** in combination with β-sitosterol was 3.4% less than control.

DETD F-**carrageenan coating** with commercial wax was less effective in respect of weight loss, as compared to above mentioned coatings.

DETD Commercially the **coating** of F-**carrageenan** in combination with β-sitosterol results in reduced losses of 36 kg per one ton of great headed garlic.

DETD Water vapor permeability was measured as described in Example 1. It was found that water vapor transmission WVT for the F-**carrageenan coating** was 453g/d n.sup.2 whereas for the F-carrageenan together with β-sitosterol the WVT decreased to 294 g/d n.sup.2.

DETD Accumulation of carbon-dioxide was measured as described in Example 1, was found to be 0.23% for the F-**carrageenan coating** and 0.4% for the K-carrageenan in combination with β-sitosterol.

DETD . . . information on the adhesion of the coating to the natural skin of the great headed garlic. Mean distances between the F-**carrageenan coating** and the great headed garlic skin were found to be 15 microns, whereas the distance between the hydrocolloid-sterol coating and. . . .

DETD Dry garlic bulbs (three months after harvest) were immersed in a warm solution (60-70° C.) containing 2% **gellan gum** (Kelcogel) and 0.01% β-stigmasterol for about 15 seconds. Excess of the gellan-sterol solution was allowed to drip and the garlic. . . .

DETD Good mechanical properties of dry films can be achieved by using **gellan gum** together with sterol. The strength (stress at failure) of this coating was about 20.3 MPa and the strain at failure. . . .

DETD Dry garlic bulbs (coated about 3 months after harvest) were immersed in a warm solution (60-70° C.), containing 2% **gellan gum** (Kelcogel), 0.01% β-stigmasterol, 0.1% Lecithin and 0.5% Locust Bean Gun for about 15 seconds. Excess of the . . . gellan-sterol-lecithin-adhesive agent solution. . . .

DETD For comparative purposes, similar dry garlic bulbs were treated in same procedure with a 2% **gellan gum** solution devoid of sterol, lecithin and Locust Bean Gun.

DETD . . . for additional 5 minutes. Cheese was kept at 4° C. and relative humidity of 75%. In the case of the **carrageenan, coating** was done at 70° C. The cold cheese immediately lowered the temperature of the coating which was later dried in.

IT 64-17-5, Ethanol, biological studies 83-46-5, β-Sitosterol 83-48-7, β-Stigmasterol 111-02-4, Squalene 814-80-2, Calcium lactate 7786-30-3, Magnesium chloride, biological studies 9000-40-2, Locust bean gum 9005-38-3, Sodium alginate 10043-52-4, Calcium chloride, biological studies 11114-20-8, κ-Carrageenan 11138-66-2, Xanthan gum 24634-61-5, Potassium sorbate 71010-52-1, Kelcogel
(protective food coating containing dried hydrocolloid gel and sterols or other natural products)

IT **71010-52-1**, Kelcogel
(protective food coating containing dried hydrocolloid gel and sterols or

L57 ANSWER 45 OF 79 USPATFULL on STN (Continued)
other natural products)

L57 ANSWER 46 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2001:315602 USPATFULL
TITLE: Non-gelatin sublatitutes for oral delivery capsules, their composition and process of manufacture
INVENTOR(S): Germadios, Aristippos, High Point, NC, United States
PATENT ASSIGNEE(S): Banner Pharmacaps, Inc., High Point, NC, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6214376	B1	20010410	<--
APPLICATION INFO.:	US 1999-142758		19980825 (9)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Page, Thurman K.			
ASSISTANT EXAMINER:	Ware, Todd S			
LEGAL REPRESENTATIVE:	Rhodes & Mason, P.L.L.C.			
NUMBER OF CLAIMS:	53			
EXEMPLARY CLAIM:	1			
LINE COUNT:	642			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Gelatin-free capsule for use in oral administration of medicines, cosmetic or bath applications, or dietary supplements can be prepared from compositions comprising

a) 8-50% by weight of water-dispersible or water-soluble plasticizer,

b) 0.5 to 12% by weight κ- **carrageenan**,

c) 0 to 60% dextrins, and

d) 1% to 95% by weight water,

with the κ-carrageenan comprising at least 50% by weight of all gums forming or contributing to formation of thermoreversible gels in the composition. A capsule for oral administration or cosmetic application may comprise a fill material to be administered to a patient

or subject and a capsule, the capsule comprising an aqueous based film comprising

a) water-dispersible or water-soluble plasticizer, and

b) carrageenan,

with the carrageenan comprising at least 50% or 75% by weight of κ-carrageenan, and the carrageenan comprising at least 50% or 75% by weight of all gums which form or contribute to the formation of thermoreversible gels. A process for forming the capsules may comprise heating the composition, casting or extruding the composition into a film, gelling the composition by cooling, associating a fill material with the gelled composition (usually as a film) and sealing the film about the fill material.

L57 ANSWER 46 OF 79 USPATFULL on STN (Continued)
DETD are present) as dispersed, e.g., at ambient. . .

Composition 1	
κ- carrageenan	4%
Maltitol syrup	30%
Sorbitol solution	2.5%
Deionized water	63.5%
Composition **2**	
κ- carrageenan	4%
Maltitol syrup	**20%**
Glycerin	11%
Deionized water	65%
Composition 3	
κ-carrageenan	4%
Potassium chloride	0.6%
Polyethylene glycol 400	6.5%
Glycerin	6.5%
Maltodextrin (ME 15)	9%
Deionized water	76.4%
Composition 4	
κ- carrageenan	4%
Maltitol syrup	**20%**
Glycerin	3%
Polyethylene glycol 400	8%
Deionized water	65%
Composition 5	
κ- carrageenan	4%
Maltitol syrup	**10%**
Sorbitol solution	6%
Deionized water	80%
Composition 6	
κ- carrageenan	4%
Maltodextrin (ME **15**)	5%
Maltodextrin (ME 18)	5%
Glycerin	6%
Polyethylene glycol 400	6%
Deionized water	76%
Composition 7	
κ-carrageenan	4%
Potassium chloride	0.6%
Glycerin	6.5%
Povidone (K-15)	6.5%
Polyethylene glycol 400	6.5%
Deionized water	76.4%
Composition 8	
κ- carrageenan	4%
Maltodextrin (ME **15**)	6%
Glycerin	6.5%
Polyethylene glycol 400	6.5%
Potassium chloride	0.6%
Gum arabic	2%
Deionized water	79.6%
Composition 9	
κ-carrageenan	3.5%
Glycerin	0%
Polyethylene glycol 400	0%
Potassium chloride	0.5%
Gum arabic	5%
Deionized water	89%

L57 ANSWER 46 OF 79 USPATFULL on STN (Continued)
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB b) 0.5 to **12**% by weight κ- **carrageenan**,
SUMM . . . has been used in wet processed photographic emulsions for more than a hundred years, it has been used to deliver **pharmaceuticals** in capsule form for more than one hundred years, it is used in cosmetics as
a binder, and is regularly. . . . . to form gels in the presence of potassium cations. These gels tend to be brittle and exhibit syneresis (contraction and **release** of entrapped liquid) as the gel shrinks. Iota Carrageenan tends to react strongly to calcium cations and forms a more.
SUMM . . . controlled melting temperature so as to soften or melt within the mouth of the consumer and providing for excellent flavor **release**, good mouth feel and sustained, timely kappa-carrageenan, and sodium salt of a sequestering agent with ionizable potassium in amounts. . . .
SUMM . . . potassium salt. Gelation is controlled so that good quality gels result by encapsulating the potassium salt in a water-soluble hydroxypropyl **cellulose**.
SUMM . . . all gums except for those from starch derivatives such as maltodextrin, gum arabic and proteins). For example, mixtures of 50/50 **κ- carrageenan**/Iota-**carrageenan**, 50/**25**/**25** **κ- carrageenan**/xanthan gum and locust bean gum, will work. Existing processing equipment for soft gelatin capsules can be used for the non-gelatin. . .
SUMM . . . (hydrocolloids) that form thermoreversible gels or contribute to the formation of thermoreversible gels include, for example, κ-carrageenan, Iota-carrageenan, xanthan gum, **gellan gum**, and mannan gums (such as locust bean gum, konjac gum, tara gum and cassia gum). The specific words used in. . . through a synergistic effect. Gums (hydrocolloids) that do not form thermoreversible gels include dextrins (including maltodextrin), proteins, gum arabic and **polyvinylpyrrolidone** (e.g., Povidone.TM.). The latter gums may simply be film formers (such as gum arabic and Povidone.TM.) or both film formers. . .
SUMM . . . present invention for the preparation of essentially gelatin-free compositions may comprise, for example, 8-50% by weight of plasticizer, 0.5 to **12**% by weight κ- **carrageenan**, and the remainder comprising water (e.g., aggregately 35% to 91.5% or 95% by weight water), exclusive of consideration of other. . . not) may be selected from mannan gums, xanthan gums, Iota-carrageenan, the native
or
modified water-soluble or water-dispersible proteins (discussed above), **gellan gums**, gum arabic, polysaccharides, Povidone.TM. (**polyvinylpyrrolidone**), natural and synthetic resins and the like. It is preferred for simplicity of the composition that these additional materials be. . . and most preferably above 6:1 or above 9:1 or higher (e.g., above 10:1). It is preferred that the use of **gellan gum** be minimized or eliminated, with less than 0.1% by weight of the composition comprising **gellan gum**, preferably less than 0.05% **gellan gum**, and most preferably 0.02% down to 0% of **gellan gum**.
DETD **1**. The κ- **carrageenan** or a blend of κ-carrageenan and Iota-carrageenan/gelling salt/mannan gum/xanthan gum (if these
materials

L57 ANSWER 46 OF 79 USPATFULL on STN (Continued)

Composition **10**	
κ- carrageenan	3.5%
Maltodextrin (DE 15)	6%
Glycerin	5%
Polyethylene glycol 400	5%
Potassium chloride	0.5%
Deionized water	80%
Composition **11**	
κ- carrageenan	3.5%
Maltodextrin (DE 15)	9.5%
Glycerin	6%
Polyethylene glycol 400	5%
Potassium chloride	0.5%
Soy protein isolate	1.5%
Deionized water	75%
Composition **12**	
κ- carrageenan	**2%**
Iota-**carrageenan**	0.5%
Locust bean gum	0.2%
Glycerin	1%
Polyethylene glycol 400	2%
Potassium chloride	0.3%
Deionized water	94%
Composition **13**	
κ- carrageenan	3%
Locust bean gum	0.3%
Glycerin	1.5%
Polyethylene glycol 400	3%
Potassium chloride	0.3%
Deionized water	91.9%
Composition **14**	
κ- carrageenan	**1.5%**
Locust bean gum	0.25%
Xanthan gum	0.25%
Glycerin	7%
Potassium citrate	0.3%
Deionized water	90.7%
Composition **15**	
κ- carrageenan	**1.5%**
Locust bean gum	0.25%
xanthin gum	0.25%
Glycerin	3.5%
Polyethylene glycol 400	3.5%
Potassium citrate	0.3%
Deionized water	90.7%
Composition **16**	
κ- carrageenan	3%
Glycerin	**1.5%**
Potassium chloride	0.45%
Polyethylene glycol 400	3.5%
Maltodextrin (DE 10)	5%
Deionized Water	86.55%

CLM What is claimed is:
. . . 1. A composition comprising: a) 8 to 50% by weight of a plasticizer; b) 0.5 to 12% by weight of κ- **carrageenan**; and c) 1 to 95% by weight water, wherein the κ-carrageenan comprises at least 50% by weight of all film-forming material in the composition and the weight ratio of plasticizer to κ- **carrageenan** is greater than 1

L57 ANSWER 46 OF 79 USPATFULL on STN (Continued)

CLM What is claimed is:
3. The composition of claim 1 wherein the ratio of plasticizer to **κ- carrageenan** is between 4:1 and 40:1.

CLM What is claimed is:
7. The composition of claim 1 further comprising less than 0.05% by weight of **gellan gum**.

CLM What is claimed is:
27. A capsule comprising a fill material and a capsule shell, said capsule shell comprising: a) a plasticizer; and b) . . . gums forming or cross-linking to the formation of thermoreversible gels in the composition and the weight ratio of plasticizer to **carrageenan** is greater than 1.

CLM What is claimed is:
25. The capsule of claim 23 wherein the capsule shell comprises less than 0.01% by weight **gellan gum**.

CLM What is claimed is:
26. The capsule of claim **23** wherein the **carrageenan** is at least 50% by weight κ-carrageenan.

CLM What is claimed is:
27. The capsule of claim 23 wherein said capsule **shell** comprises said plasticizer and **carrageenan** in a ratio greater than 4:1, plasticizer to **κ- carrageenan**.

CLM What is claimed is:
28. The capsule of claim 26 wherein said capsule **shell** comprises said plasticizer and **κ- carrageenan** in a ratio greater than 4:1, plasticizer to **κ- carrageenan**.

CLM What is claimed is:
73. The composition of claim 1 further including at least one non-thermoreversible gum selected from the group consisting of hydrolyzed starches, dextrins, proteins, gum arabic, and **polyvinylpyrrolidone**.

CLM What is claimed is:
74. The capsule of claim 23 further comprising a hydrolyzed starch present in an amount from 0.5 to 15% by weight of **carrageenan**.

CLM What is claimed is:
35. A composition comprising: a) 8 to 50% by weight of a plasticizer;
b) 0.5 to 12% by weight **carrageenan**; c) 0 to 60% by weight of at least one non-thermoreversible gum; and d) 0.5 to 95% by weight water, . . . comprises at least 50% by weight of all film-forming material in the composition and the weight ratio of plasticizer to **carrageenan** is greater than 1.

CLM What is claimed is:

L57 ANSWER 47 OF 79 USPATFULL on STN
ACCESSION NUMBER: 2000:135456 USPATFULL
TITLE: Microencapsulation and electrostatic processing method
INVENTOR(S): Morrison, Dennis R., Kenai, TX, United States
Mosier, Benjamin, Houston, TX, United States
The United States of America as represented by the Administrator of the National Aeronautics and Space Administration, Washington, DC, United States [U.S. government]

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6103271		20000815
APPLICATION INFO.:	US 1998-79770		19980515 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-349169, filed on 2 Dec 1994, now patented, Pat. No. US 5827531		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Speer, James M.		
LEGAL REPRESENTATIVE:	Cate, James M.		
NUMBER OF CLAIMS:	52		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	15 Drawing Figure(s); 5 Drawing Page(s)		
LINE COUNT:	2470		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods are provided for forming spherical multilamellar microcapsules having alternating hydrophilic and hydrophobic liquid layers, surrounded by flexible, semi-permeable hydrophobic or hydrophilic outer membranes which can be tailored specifically to control the diffusion rate. The methods of the invention rely on low shear mixing and liquid-liquid diffusion process and are particularly well suited for forming microcapsules containing both hydrophilic and hydrophobic drugs. These methods can be carried out in the absence of gravity and do not rely on density-driven phase separation, mechanical mixing or solvent evaporation phases. The methods include the process of forming, washing and filtering microcapsules. In addition, the methods contemplate coating microcapsules with ancillary coatings using an electrostatic field and free fluid electrophoresis of the microcapsules. The microcapsules produced by such methods are particularly useful in the delivery of **pharmaceutical** compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . and free fluid electrophoresis of the microcapsules. The microcapsules produced by such methods are particularly useful in the delivery of **pharmaceutical** compositions.
SUMM The present methods are directed to the formation of multi-layered, microcapsules containing a variety of compounds, including **pharmaceuticals**. The present methods rely on controlling fluid shear forces in the microcapsule forming solutions. This low-shear approach to microcapsule formation. . . . for coating microcapsules with polymeric coatings. One such method involves the use of electrostatic fields to facilitate coating microcapsules with **polyvinyl** pyrrolidone.
SUMM . . . limitations is encapsulation into microcapsules or liposomes. Encapsulation of therapeutics can enable delivery to target organs where

L57 ANSWER 48 OF 79 USPATFULL on STN (Continued)
79. The composition of claim 39 comprising less than 0.05% by weight of **gellan gum**.

CLM What is claimed is:
41. The composition of claim 35 wherein the at least one non-thermoreversible gum is selected from the group consisting of hydrolyzed starches, dextrins, proteins, gum arabic, and **polyvinylpyrrolidone**.

CLM What is claimed is:
. . . for preparing a non-gelatin composition comprising: a) dispersing **κ-carrageenan** into a plasticizer such that the weight ratio of plasticizer to **κ- carrageenan** is greater than 1; b) adding an aqueous solution; c) heating and stirring the **κ-carrageenan**, plasticizer, and aqueous solution mixture; and d) cooling the. . .
37 50-70-4, Sorbitol, Biological studies 56-81-5, Glycerin, Biological studies 87-99-0, Xylitol 585-86-4, Lactitol 585-88-6, Maltitol 9004-57-3, Dextrin 9050-36-6, Maltodextrin 11114-20-8, **κ-Carrageenan** **71010-52-1, Gellan gum**
(non-gelatin substitutes for oral delivery capsules)
37 **71010-52-1, Gellan gum**
(non-gelatin substitutes for oral delivery capsules)

L57 ANSWER 48 OF 79 USPATFULL on STN (Continued)
they can be **released**. Incorporation of therapeutics into microcapsules facilitates delivery by parenteral injection, nasal inhalation and dermal administration and provides for sustained drug **release**.
SUMM . . . bilayers when dispersed in aqueous solutions at concentrations at or above their critical micelle concentrations. Typically, in liposomes that carry **pharmaceuticals**, the **pharmaceutical** is dissolved in the aqueous phase. However, drugs of limited solubility in aqueous solvents are difficult to incorporate into liposomes.. . .
SUMM Other solid-matrix approaches have utilized copolymers such as **polyvinyl** chloride/acrylonitrile dissolved initially in organic solvents to form microparticles containing aqueous enzyme solutions. U.S. Pat. No. 3,639,306 to Sternberg et.
SUMM . . . thereby limiting the packing density. Additionally, many drugs cannot be trapped or adsorbed in these systems at effective concentrations and drug-**release** rates are often not constant.
SUMM . . . as phosphatidyl ethanolamine derivatized with polyethyleneglycol). U.S. Pat. No. 5,225,212 to Martin et al. discloses a liposome composition for extended **release** of a therapeutic compound into the bloodstream, the liposomes being composed of vesicle-forming lipids derivatized with a hydrophilic polymer, wherein the liposome composition is used for extending the period of **release** of a therapeutic compound such as a polypeptide, injected within the body. Formulations of "stealth" liposomes have been made with. . .
SUMM . . . form the liposomes, 2) remove unwanted organic solvents, detergents, and 3) harvest the proper size and shape microparticles for optimum **pharmacologic** efficacy [Talsma and Crommelin 1992]. Also conventional liposomes often use natural lipids and lecithins (from eggs, soybeans and other inexpensive. . . . the liposomes from the circulatory system before they arrive at the target tissue. This creates variable dose-responses making calculations of **pharmacokinetic** and therapeutic doses very difficult [Allen 1988]. Major difficulties with commercial preparation of microcapsules often involve density-driven phase separation of.
SUMM . . . both the aqueous and lipid phases in order to outward) diffuse. This limits the type of drugs that can be **released** from conventional liposomes and the mole ratio of aqueous to lipid phases limits the amount of liquid drug that can. . .
SUMM . . . than 1 micron can be coated. Microcapsules produced by such improved methods would be particularly useful in the delivery of **pharmaceutical** compositions.
SUMM . . . coat microcapsules having diameters greater than 1 micron. Microcapsules produced by such improved methods are useful in the delivery of **pharmaceutical** compositions.
SUMM . . . can be used for intravenous administration of drugs. Microcapsules having diameters of over 300 microns are useful in formulations of **pharmaceutical** compounds for intraperitoneal administration. Generally, smaller microcapsules are made when shearing forces are larger. The use of increasing amounts of
SUMM . . . layers alternate between hydrophobic and hydrophilic. For example, a hydrophilic aqueous layer could be surrounded by a hydrophilic layer containing **polyvinyl** pyrrolidone.
SUMM . . . also contain about 1-10% water by volume. The primary solution may serve as a carrier for chemical additives such as **pharmaceuticals** or other bioactive compounds or commercially desirable compounds that can be used to modify the characteristics of the microcapsule in. . .
SUMM . . . the groups listed in Table I. The secondary solution also serves as a carrier solution for chemical additives such as

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pharmaceuticals or other bioactive or commercially desirable compounds which can be added to the secondary solution up to the solubility limit . . .

SUMM . . . TABLE II

FORMULATION OF HYDROPHILIC SECONDARY SOLUTION

Solvent (70-90%)	Polymer (1-20%)
Water	Polyethylene glycol (PEG 400-20000) (polysaccharides) MW 4000-100000
Surfactant (1-20%)	(HLB > 10) **polyvinylpyrrolidone** (PVP)
Sorbitan monooleate	Ethe ethylene oxides
	polyvinyl alcohols
Deatran	**polyvinyl** acetate
PEG	(hydrocolloids)
C.sub.12 -C.sub.20	fatty acids
	gelatin
quaternary NH.sub.4	gum tragacanth
ethoxylated salts	**carrageenans**
2-amino-**2**-methyl-propanol	karaya gum
	guar gum
Salt (1-78 weight/volume)	(alginates)
NaCl	**(celluloses)**
KCl	carboxymethyl **cellulose**
CaCl.sub.2	hydroxyethyl **cellulose**
Quaternary ammonium salts	hydroxypropyl **cellulose**
cetyl trimethylammonium bromide	
Phosphate buffered saline (PBS)	
	Dissolved chemical
4-methoxy-4-(3-phosphatidyl choline)	
	(to saturation as desired)
spiro [1,2-dioxetane-3,-y,1-adamantane] disodium salt	

SUMM . . . TABLE III

FORMULATION OF HYDROPHILIC PRIMARY SOLUTION

Solvent (70-90%)	Hydrophilic Polymer
water	**polyvinylpyrrolidone** (PVP)
	polyvinyl alcohols
Co-solvents (0-20%	
	polyvinyl acetate
C.sub.3 -C.sub.8	alcohols
	propylene glycol
tetrahydrofuran (THF)	(hydrocolloids)

L57 ANSWER 47 OF 79 USPATFULL on STN (Continued)
produced by the present methods is described in more detail in the parent patent, U.S. Pat. No. . . .

SUMM . . . are of particular utility when formulating organic-soluble drugs as these types of drugs are otherwise very difficult to administer. The **pharmaceuticals** may be those selected from the group of such widely diversified **pharmaceutical** compositions as cytotoxins, proteases, cytokines, anti-parasants, steroids, anti-fungal agents, fibrinolytic enzymes, and antibiotics. The inventors have successfully encapsulated representatives of these classes of **pharmaceuticals** using the methods of the invention.

SUMM . . . when microcapsules having hydrophobic outer skins are made, hydrophilic barriers are preferred. Examples of hydrophilic porous barriers are ceramics, glass, **polyvinyl** acetate and **cellulose** filters. In certain circumstances a barrier made of **cellulose** acetate may be used. This material is an intermediate material having both hydrophobic and hydrophilic characteristics and can be wet. . . .

SUMM . . . mmho/cm, for example, 2.5 mM potassium phosphate, 1% amphol

ines (LKB) and a density gradient made of 0-20% ficoll (MW 400,000 **Pharmacia**) or 0-8% sucrose. In this method typical electric field strengths are in the range of 4-6 volts/cm with a resulting. . . .

SUMM . . . TABLE VII

COATING COMPOSITIONS

	cationic	
Anionic coatings		
	coatings	zwitterions
Polyvinyl pyrrolidone		
	polybutidine	
		phosphatidyl choline
Polyvinyl acetate		
	polylysine	dipalmityl
Phosphatidyl serine		
	polyarginine	
		phosphatidyl
Phosphatidyl glycerol		
	stearylamine	
		choline
beef heart cardiolipin		
	protamine	cyclodextrins
fabronectin	trypsin	carbomethyrin acid
laminin	lysozyme	amphoterins
collagen	glycoproteins	
		ampholytes

Eqp. . .

SUMM Coatings may be used to add **pharmaceutical** compositions to the formed surfaces of the microcapsule. Instances of this include coating with immunoglobulins, other proteins, hydrocolloids or polysaccharides. . . . may be selected from the group of such hydrocolloids consisting of collagen, isoelectric gelatin, agar, gum arabic, gum tragacanth, alginates, **cellulose** derivatives and **carrageenans**. In some instances the **coating** fluid comprises an oil or C.sub.14 -C.sub.60 paraffin for coating the formed microcapsules. Regardless of what coating material is

desired, . . .

SUMM Coating compositions may also contain a chemical activator which can act

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dioxane	gelatin
acetonitrile	gum tragacanth
dimethylformamide (DMF)	
	gum arabic
dimethyl sulfoxide (DMSO)	
	gum accasnsa
	carrageenans
	karaya gum
Oil (1-10%)	guar gum
lodinated poppy seed oil	(PIPO)
	(alginates)
mineral oil	**(celluloses)**
cotton seed oil	carboxymethyl **cellulose**
olive oil	hydroxypropyl **cellulose**
safflower oil	carboxypropyl **cellulose**
canola oil	hydroxyethyl **cellulose**
peanut oil	(phospholipids)
sesame oil	(lecithins)
corn oil	phosphatidyl choline
	(polysaccharides)

Dissolved compounds

	corn starch
(to saturation as desired)	
	cyclodextrins
	dextrans

SUMM . . . polyethyleneglycol 400-20000 daltons (Da), dextran ranging from

4000 to 100,000 in molecular weight more preferably 40,000 to 70,000 molecular weight, **polyvinyl** pyrrolidone, **polyvinyl** alcohols, **polyvinyl** acetate, gelatin, gum tragacanth, carrageenans, Karaya gum, Guar gum, gum arabic, alginates, carbomyrthy **cellulose**, hydroxypropyl **cellulose**, carboxypropyl **cellulose**, lecithins and the like. Although the term polymer and surfactant are used in the Tables with distinct compositions, it is. . . .

SUMM . . . X makes reference to the critical components of the formulations without providing a comprehensive list of each ingredient. For example, **pharmaceutical** compositions and oils are also incorporated into that formulation but are not specifically referenced. Considerations for selecting these components are. . . . skin is selected so that it will dissolve in physiological body fluids.

Suitable

polymers for this purpose include polyethylene glycol, **polyvinyl** alcohol, **polyvinyl** chloride, **cellulose** acetate, lecithin, gum arabic, gum karaya, gum tragacanth, sodium alginate

SUMM Certain methods of the present invention provide for the incorporation of **pharmaceutical** compositions into microcapsules. In these methods, the **pharmaceutical** composition is introduced into at least one of the solutions used to formulate the microcapsule layers. In some cases, the. . .

. . . same microcapsule, e.g. antibiotics and immuno-stimulants to treat

resistant infections or multiple fibrinolytic drugs to dissolve emboli. The incorporation of **pharmaceutical** compounds in microcapsules

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on inactive forms of the **pharmaceutical** agents such as proteins (drug) as they diffuse out of the microcapsule. This is illustrated when the **pharmaceutical** is a pro-enzyme and where the activator is another proteolytic enzyme which cleaves the pro-enzyme at active site to render. . . .

SUMM In a preferred electrostatic microcapsule coating method microcapsules are placed in a solution containing 0.1% to 0.5% **polyvinyl** pyrrolidone (PVP) in water or in the primary solution and an electric field of 10 Volts/cm applied to the suspension. In such a method the PVP diffuses through the solution and coats microcapsules having a positive surface charge. Alternatively, **polyvinylacetate** can be used as the coating material in analogous methods.

SUMM . . . electrostatic coating process. One such method involves placing

the microcapsules in a coating solution consisting of approximately 0.1%

to 0.5% **polyvinyl** pyrrolidone dissolved in a solution having a high resistance to current flow. An electric field of approximately 10 volts/cm is

DETD . . . surface area ratio in order to control the rate of diffusion of

a solute in such spheroids. In particular, sustained **release** of **pharmaceuticals** contained in such spheroids within microcapsules may find utility.

DETD **Polyvinyl** pyrrolidone (PVP) and a commercial lecithin (CENTROLEX-F,TM. by U.S.Soya, Inc.) were used to form multi-lamellar microcapsules at 20°C. Fluorescent

DETD . . . tumor. Multi-layered microcapsules have been developed which can provide a new intravascular delivery system for targeted tissues and

sequential, sustained **release** of multiple anti-tumor drugs. This method has resulted in formation of flexible spherical microcapsules of more uniform size, which can

DETD . . . nasal or buccal mucosa or via inhalation directly to the lungs.

Examples include protected delivery of neucolytic DNAse for sustained **release** treatment of cystic fibrosis and 3 anti-trypsin for patients with deficiencies in the lung epithelium.

DETD . . . polyethylene glycol). A polysaccharide (Dextran) and normal saline (0.9%) are added which helps achieve the desired critical micelle

concentration. A **pharmaceutical** soluble in water is added. An example is:

DETD (according to required dose and **release** rate)
DETD (according to required dose and **release** rate)
DETD

An example is:

	5% **polyvinyl** alcohol dissolved in a
	mixture of
	25% isopropyl alcohol and
	80% water

DETD . . . moles Ethylene oxide
Water (up to 100% volume)
dissolved dry at saturated or specified concentration
(according to required dose and **release** rate)

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DETD 1% **Polyvinyl** pyrrolidone
DETD In preferred methods the microcapsules are electrostatically coated with
a polymeric coating such as **polyvinyl** pyrrolidone or **polyvinyl** acetate or other coating solutions. This coating process greatly strengthens the microcapsules. The coating solution is 0.1% to 0.5% by . . . of the polymer in a solvent having high resistance to current flow. One suitable solution is a 0.1% solution of **polyvinyl** pyrrolidone in water. The coating solution is introduced into the microcapsule containing chamber from reservoir F as shown in FIG8.. . .

DETD . . . suitable electric field is 10-40 volt/cm. In methods that involve the use of negatively charged polymeric coating compounds such as **polyvinyl** pyrrolidone, the cathode is located in the first chamber and the anode is placed in the second chamber so that. . .

DETD
Primary 1 mg/ml Keglan
Solution:
1% Polyethylene Glycol-4000
1% Dextran-40
1% Sorbitin monooleate with 20 moles ethylene oxide (Tween 80)
0.1% **Polyvinyl** pyrrolidone (PVP-K90)
0.02% Cy-3 Fluorescent dye
Secondary
5% w/w Glycerol monostearate (polyoxacharide mixture,
Solution:
Eastman 1900) dissolved in the following:
92% Isopropyl. . .

DETD Allen, T. M., Mehra, T., Hansen, C. and Chin, Y.C., Stealth Liposomes: An Improved Sustained **Release** System for 1-b-D-Arabinofuranosylcytosine, Cancer Res. 52:2431-39, 1992.

DETD Gabizon, A., et al., Liposome-Associated Doxorubicin: Preclinical **Pharmacology** and Exploratory Clinical Phase, in G. Lopez-Berestein and A.C. Fidler (Eds.) Therapy of Infectious Diseases and Cancer, Alan R.

DETD Talsma, H. and Crommelin, D. J. A., Liposomes as Drug Delivery Systems, Part 1: Preparation. **Pharmaceutical** Technology, pp. 96-106, October 1992.

CLM What is claimed is:
. . . glycerol monooleate and wherein said step for formulating a secondary
solution further comprises the step of preparing a mixture comprising **polyvinyl** pyrrolidone and ethoxylated (4) sorbitan monostearate.

CLM What is claimed is:
27. The method of claim 22 further comprising the steps of formulating a
coating solution, by dissolving **polyvinyl** pyrrolidone in said solution, adding said coating solution to said coated microcapsules, applying an electric field to said coating solution. . . .

CLM What is claimed is:
28. The method of claim 22 further comprising the steps of formulating a

L57 ANSWER 48 OF 79 USPATFULL on STN
ACCESSION NUMBER: 1999:163424 USPATFULL
TITLE: Solid medium for amplification and expression of nucleic acids as colonies
INVENTOR(S): Chetverin, Alexander Borisovich, Puschino, Russian Federation
Chetverina, Helena Vladimirovna, Puschino, Russian Federation
PATENT ASSIGNEE(S): Institut Belka, Puschino, Russian Federation (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6001569		19991214	<--
APPLICATION INFO.:	US 1996-723260		19960930 (8)	<--
RELATED APPLN. INFO.:	Division of Ser. No. US 1992-966713, filed on 26 Oct 1992, now patented, Pat. No. US 5616478			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Campbell, Eggerton A.			
LEGAL REPRESENTATIVE:	Fish & Richardson, P.C.			
NUMBER OF CLAIMS:	26			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	10 Drawing Figure(s); 4 Drawing Page(s)			
LINE COUNT:	2529			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Amplification and/or expression of nucleic acids is carried out in a medium immobilized by using an organic and/or inorganic solid matrix penetrating the medium and having a porous, fibrous, reticulated, coiled, capillary, lamellar or folded texture and which includes the components of a cell-free enzyme system of exponential amplification of nucleic acids and/or components of a cell-free enzyme system of nucleic acid expression. In this medium, the progeny of each molecule (clone) and the expression products remain in the same zone of the reaction volume where the matrix molecule was initially located. The method permits cloning of nucleic acids in vitro as well as detection of solitary nucleic acid molecules in the sample studied.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . or cell immobilization, as well as for growing bacteria, cells and viruses; such as agarose, polyacrylamide, nylon, gelatin, alginate, carrageenan, **cellulose**, silica gel, titanium sponge, cross-linked agarose, dextran or polyethylene glycol, and their combinations and derivatives are suitable [Primrose, S. B. . . . For example, temperature-resistant matrix should be used to carry out PCR. In this case, matrices such as comprised of polyacrylamide, **cellulose**, polyamide (nylon), or of cross-linked agarose, dextran or polyethylene glycol, are appropriate.

DETD . . . the medium is immobilized, or the reaction substrate(s) in a chemically unavailable "caged" form, which can be decomposed to **release** the normal substrate(s). An example of caged substrate is a photosensitive derivative of ATP, wherein the y-phosphate is modified with a 1-(2-nitro)phenylethyl group [Kaplan, J. H., Forbush, B., III, and Hoffman, J. F. (1978). Rapid Photolytic **Release** of Adenosine 5"-Triphosphate from a Protected Analogue: Utilization by the Na:K Pump of Human Red Blood Cell Ghosts. Biochemistry 17, . . .

DETD . . . with polyethylene imine. Roche, C. (1987). Cell Immobilization

L57 ANSWER 47 OF 79 USPATFULL on STN (Continued)

coating solution, by dissolving **polyvinyl** acetate in said solution, adding said coating solution to said coated microcapsules, applying an electric field to said coating solution. . . .

CLM What is claimed is:
. . . a primary solution by preparing a mixture containing 1 mg/ml Keglan, 1% polyethylene glycol-600, 1% dextran-40, 1% Tween 80, 0.5% **polyvinyl** pyrrolidone, 0.05% Cy-3 fluorescent dye; formulating a secondary solution by preparing a mixture containing 5% glycerol monostearate,

92% isopropyl alcohol,. . .

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in Calcium Alginate. Methods Enzymol. 135, 175-189. The granules can also be **coated** with kappa-**carrageenan** [Chibata, I., Tosa, T., Sato, T. and Takata, I. (1987). Immobilization of Cells in **Carrageenan**. Methods Enzymol. **135**, **189**-198), or with **cellulose** nitrate, nylon, and other types of semipermeable membranes [Chang, T. M. S. (1976). Microencapsulation of Enzymes and Biologicals. Methods Enzymol. . . .

DETD (b) Enzyme and/or substrate entrapment by impregnating a pre-formed solid matrix.--Fibrous thin layers, such as those based on **cellulose** or nylon, or porous layer such as based on silica gel or titanium sponge, are easy to prepare by soaking. . . .

DETD . . . dextrans with epichlorohydrine or with N,N'-methylene bisacrylamide [Flodin, P. (1962). Dextran Gels and Their Applications in
Gel Filtration, Dissertation, AB **Pharmacia**, Uppsala, Sweden; Ostesman (1986), supra]. However, in most cases cross-linking occurs under conditions that cannot be tolerated by the enzymes. . . .

DETD . . . treated with 5 M guanidine isothiocyanate solution, that results in the lysis of cells, denaturing of proteins (including nucleases), and **release** from cellular debris and denaturation of RNA and DNA [Pellegrino, M. G., Lewis, M. Meyer, W. A., III, Lazowski, R. . . . Employing dA-tailed Capture Probes. I. Multiple Capture Methods. Anal. Biochem. 181, 345-359]. After washing the beads, the target molecules are **released** into solution by heating in a low-salt buffer and used as templates for generation of a replicable reporter from binary.

DETD . . . DNA targets. The extended sequence includes a copy of the target region (dashed line). The extended first probe is then **released** from the target, permitting its hybridization to a second probe (middle diagram) that contains the second probe sequence and a. . .

DETD . . . D. C. (1992). Rapid and Sensitive Colorimetric Method for Visualizing Biotin-labeled DNA Probes Hybridized to DNA or RNA immobilized on **Nitrocellulose**: Bio-blots. Proc. Natl. Acad. Sci. U.S.A. 80, 6045-6049]. Gamez encoding. photoproteins such as apo-obelin (from hybrid Obelia geniculata) can be. . .

CLM What is claimed is:
. . . to claim 1, wherein said solid matrix is selected from the group consisting of agarose, polyacrylamide, nylon, gelatin, alginate, carrageenan, **cellulose**, silica gel, titanium sponge, dextran, and polyethylene glycol.

CLM What is claimed is:
. . . to claim 11 wherein said solid matrix is selected from the group consisting of agarose, polyacrylamide, *nylon*, gelatin, alginate, carrageenan, **cellulose**, silica gel, titanium sponge, dextran, and polyethylene glycol.

CLM What is claimed is:
. . . matrices of said first and second layers are selected from the group consisting of agarose, polyacrylamide, *nylon*, gelatin, alginate, carrageenan, **cellulose**, silica gel, titanium sponge, dextran, and polyethylene glycol.

L57 ANSWER 49 OF 79 USPATFULL on STN
ACCESSION NUMBER: 1999:161737 USPATFULL
TITLE: Extremely high density barium suspension as a contrast medium for upper gastrointestinal examination
INVENTOR(S): Sirai, Kazuo, Kyoto-fu, Japan
PATENT ASSIGNEE(S): Fushimi Pharmaceutical Co., Ltd., Kagawa-ken, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5921234		19990713	<--
APPLICATION INFO.:	US 1996-740501		19961105 (8)	<--
	NUMBER	KIND	DATE	
PRIORITY INFORMATION:	JP 1995-345032		19951208	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Hollinden, Gary E.			
LEGAL REPRESENTATIVE:	Ostrolenk, Faber, Gerb & Soffen, LLP			
NUMBER OF CLAIMS:	6			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	11 Drawing Figure(s); 10 Drawing Page(s)			
LINE COUNT:	2218			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB To provide a barium power preparation and application thereof to an extremely high density barium suspension, processes for producing them, and a method of upper gastrointestinal examination, wherein double contrast radiography can be carried out on-the-fly without the use of a gastric tube and the injection of any parasympatholytic, only by one slow rolling operation with the patient on the table. A barium power preparation obtained by mixing specified proportions of large, medium and small component particles which are produced from large, medium and small particles of pure barium sulfate having specific particle properties, by adding Gum Tragacanth and Carrageenan in specified amounts and at a specified ratio, kneading their mixture under specified kneading conditions to fragment the molecules of Gum Tragacanth and **Carrageenan** and **coat** the particles with them, and drying and sterilizing the particles, and a barium suspension prepared by suspending the above barium power preparation in water at an extremely high density are used.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . and at a specified ratio, kneading their mixture under specified kneading conditions to fragment the molecules of Gum Tragacanth and **Carrageenan** and **coat** the particles with them, and drying and sterilizing the particles, and a barium suspension prepared by suspending the above barium

SUMM . . . has long been awaited, as no ideal barium is commercially available yet. Although new products claiming "high density" have been

L57 ANSWER 49 OF 79 USPATFULL on STN (Continued)
Sulfate 26% approx. 35% approx. 31% approx.
group
X/6-anydro 29 to 28% 0 to 2%. . . effectively K ion tively by Ca ion by X ion
Chara- Fragile, Large Not gelled Elastic, Small water
teristics water **release**- **releasable**, of gel able heat- heat-reversible reversible
Solubility Swells but All metallic Calcium salt makes to cold insoluble. salts are thixotropic
. . .
DETD . . . particles, the content of Gun Tragacanth and Carrageenan are 0.01% and 0.1%, respectively [ratio of contents of Gum Tragacanth and **Carrageenan is 1:10**], the effective Gum Tragacanth content for **Carrageenan** is **0.15**[1.2 to 0.05% 0.05%. Thus, the effective Gum Tragacanth content of the composite additive in the large particles is 0.025+0.005=0.075% (see Table 2).
DETD In the medium particles, the ratio of the Gum Tragacanth content and the **Carrageenan** content is approximately **1:10**. Therefore, in order to attain the effective Gum Tragacanth content of the medium particles, 0.25%, the Gum Tragacanth content in.
DETD In the small particles, the ratio of the Gum Tragacanth content and the **Carrageenan** content is approximately **1:1**. Therefore, in order to attain the effective Gum Tragacanth content of the small particles, 0.5%, the Gum Tragacanth content in. . . .
CLM What is claimed is:
. . . particle size distribution, and said effective Gum Tragacanth contents are calculated using the following formula Effective Gum Tragacanth content=[Gum Tragacanth content]×[**Carrageenan** content]× **1/2.5**, [wherein the contents is expressed in weight percent, and the viscosity reduction effect of Gum Tragacanth is assumed as 2.5. . .

L57 ANSWER 50 OF 79 USPATFULL on STN (Continued)
released for the last few years, their densities in practical use are only about 200 W/V%, and fall short of addressing
SUMM . . . cutting the argument by K. Miller, that "regrettably they generally do not meet the standard purity of the medical literature (**Pharmacopoeia**) as they contain excessive amounts of heavy metals."
SUMM . . . at a specified ratio, kneading the mixture under specified kneading conditions to fragmentize the molecular chains of Gum Tragacanth and **Carrageenan** and **coat** the particles with them, and drying and sterilizing them; a barium suspension prepared by suspending said barium powder preparation in. . . .
SUMM Effective Gum Tragacanth content [Gum Tragacanth content]×[**Carrageenan** content]× **1/2.5**,
. . . furnaces. The chemical composition and purity of pure barium sulfate used as the material is strictly controlled by the Japanese **Pharmacopoeia**. However, physical properties such as particle size or viscosity are hardly controlled. As a result, variation in physical properties by. . . .
SUMM . . . Practical content

Effective Gum
Particle size peak area and its ratio To Gum Tragacanth Tragacanth
content and Viscosity
size (μm) (n.sup .**2** /g) C: **Carrageenan** its ratio (%;mPa.sp)

Large
8.0 0.23 1.0 7 0.05% + C 0.15% 1.0 16

Medium 2.0 about 2.5 0.644 about 0.75% 2.8 about 3.3 7 0.05% 0.15% 1.0 16

DETD . . . Tragacanth and Carrageenan, and kneaded under specified conditions, in order to fragment adequately the molecules of the Gum Tragacanth and **Carrageenan** and **coat** the particles with them, to make the viscosity as low as possible. The large, medium and small particles, whose viscosity.
DETD Gum Tragacanth is composed mainly of Tragacanthic acid and Bassorin, as well as of water (16%), **cellulose** (4%), starch (3%), and minerals (3%). The main component, Tragacanthic acid, is a mixture of acidic polysaccharides consisting of furose, . . .
DETD . . . suitably used for the present invention is Jenugel CJ (Copenhagen Pectin Co., Inc.), in which k fraction accounts for about 1/3 of the **Carrageenan**. It is a gelled mixture intended originally for fruit jelly and contains a large amount of impurities as proved. . . . applications when discussing the character of medicines: A crude drug may sometimes be superior in practice because of
Its milder **pharmacological** effect than a pure synthetic cardiac.

TABLE 1
DETD
Classification and Characteristics of Carrageenan
κ-Carrageenan
Carrageenan
ι- **Carrageenan**
Galactose
29% approx. 45% approx. 20% approx.

L57 ANSWER 50 OF 79 USPATFULL on STN
ACCESSION NUMBER: 1999:113709 USPATFULL
TITLE: Method for amplification and expression of nucleic acids in solid media and its application for nucleic acid cloning and diagnostics
INVENTOR(S): Chetverin, Alexander Borisovich, Moskovskaya oblast, Russian Federation
Chetverina, Helena Vladimirovna, Moskovskaya oblast, Russian Federation
PATENT ASSIGNEE(S): Institut Belka, Russian Federation (non-U.S. government)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5958698		19990928	<--
APPLICATION INFO.:	US 1995-354446		19981117 (9)	<--
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-723260, filed on 30 Sep 1996 which is a division of Ser. No. US 1992-966713, filed on 26 Oct 1992, now patented, Pat. No. US 5614478			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Campbell, Eggerton A.			
LEGAL REPRESENTATIVE:	Fish & Richardson P.C.			
NUMBER OF CLAIMS:	25			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	10 Drawing Figure(s); 4 Drawing Page(s)			
LINE COUNT:	3556			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Amplification and/or expression of nucleic acids is carried out in a medium immobilized by using an organic and/or inorganic solid matrix penetrating the medium and having a porous, fibrous, or laminated, coiled, capillary, lamellar or folded texture and which includes the components of a cell-free enzyme system of exponential amplification of nucleic acids and/or components of a cell-free enzyme system of nucleic acid expression. In this medium, the progeny of each molecule (clone) and the expression products remain in the same zone of the reaction volume where the matrix molecule was initially located. The method permits cloning of nucleic acids in vitro as well as detection of solitary nucleic acid molecules in the sample studied.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . or cell immobilization, as well as for growing bacteria, cells and viruses; such as agarose, polyacrylamide, nylon, gelatin, alginate, carrageenan, **cellulose**, silica gel, titanium sponge, cross-linked agarose, dextran or polyethylene glycol, and their combinations and derivatives are suitable [Primrose, S. B . . . For example, temperature-resistant media should be used to carry out PCR. In this case, matrices such as comprised of polyacrylamide, **cellulose**, polyamide (nylon), or of cross-linked agarose, dextran or polyethylene glycol, are appropriate.
DETD . . . the medium is immobilized; or having the reaction substrate(s) in a chemically unavailable "caged" form, which can be decaged to **release** the normal substrate(s). An example of caged substrate is a photosensitive derivative of ATP, wherein the γ-phosphate is modified with a 1-(2-nitrophenyl)ethyl group [Kaplan, J. H., Forbush, B., III, and Hoffman, J. F. (1978). Rapid Photolytic **Release** of

L57 ANSWER 50 OF 79 USPATFULL on STN (Continued)
Adenosine 5'-Triphosphate from a Protected Analogue: Utilization by the Na/K Pump of Human Red Blood Cell Ghosts. Biochemistry 17,
DETD . . . with polyethylene imine. Roche, C. (1987). Cell Immobilization in Calcium Alginate. Methods Enzymol. 135, 175-189. The granules can also be **coated** with kappa-**carrageenan** (Chibata, I., Tosa, T., Sato, T. and Takata, I. (1979). Immobilization of Cells in **Carrageenan**. Methods Enzymol. 135, **189**-198), or with **cellulose** nitrate, nylon, and other types of semipermeable membranes (Chang, T. M. S. (1976). Microencapsulation of Enzymes and Biological. Methods Enzymol. . .

DETD (b) Enzyme and/or substrate entrapment by impregnating a pre-formed solid matrix.--Fibrous thin layers, such as those based on **cellulose** or nylon, or porous layer such as based on silica gel or titanium spongra, are easy to prepare by soaking . . . mentans with epichlorohydrine or with N,N'-methylene bisacrylamide (Floditz, K. (1982). Beaten Gels and Their Applications in Gel Filtration, Dissertation, AB **Pharmacia**, Uppsala, Sweden; Ostsman (1986), supra). However, in most cases cross-linking occurs under conditions that cannot be tolerated by the enzymes.

DETD . . . treated with 5 M guanidine isothiocyanate solution, that results in the lysis of cells, denaturing of proteins (including nucleases), and **release** from cellular debris and denaturation of DNA and RNA (Pellegrino, M. G., Lewis, M. Meyer, W. A. III, Lanzotti, E. . . . Employing ds-tailed Capture Probes. I. Multiple Capture Methods. Anal. Biochem. 157, 341-347. After washing the beads, the target molecules are **released** into solution by heating in a low-salt buffer and used as templates for generation of a replicatable reporter from binary.

DETD . . . DNA targets. The extended sequence includes a copy of the target region (dished line). The extended first probe is then **released** from the target, permitting its hybridization to a second probe (middle diagram) that contains the second probe sequence and a.

DETD . . . S. C. (1993). Rapid and Sensitive Colorimetric Method for Visualizing Biotin-labeled DNA Probes Hybridized to DNA or RNA Immobilized on **Nitrocellulose**: Bio-blots. Proc. Natl. Acad. Sci. U.S.A. 90, 4045-40491. Genes encoding photoproteins such as apo-obelin (from hydroid Obelia geniculata) can be. . .

CLM What is claimed is:

the . . . wherein said solid surfaces comprise a solid matrix selected from the group consisting of agrose, polyacrylamide, nylon, gelatin, alginate, carrageenan, **cellulose**, silica gel, titanium spongs, dextran, and polyethylene glycol.

L57 ANSWER 51 OF 79 USPATFULL on STN (Continued)
polyethersetes, polyamids, hydrogels, **cellulose**, polypeptides, polyaminotriazoles, and albumin beads. Therapeutic agents investigated for delivery from polymeric matrices include narcotic antagonists (naloxone), steroids, antimalarials, insulin,

SUM04 Active ingredients which are required to be **released** in different parts of the alimentary tract may be coated or packaged in materials which react differently with body fluids.

SUM04 Furthermore, trace amounts of formaldehyde in foods and **pharmaceuticals** because of the toxic properties of this substance also raises problems with food and drug administration authorities.

SUM04 . . . a mixture of gelatin and alkali metal salt of a partial ester of a polyoxyhexoylic acid and a suitable **cellulose** ether. For example, a solution of sodium carboxymethyl which cellacephate was dissolved was mixed with gelatin. Capsules were then

SUM04 Derivatives of **cellulose** with enteric properties have also been developed. An example of this is U.S. Pat. No. 3,826,666 which refers to a.

SUM04 Enteric capsules produced from polymers not based on **cellulose** have also been developed. For example, JP 7310522 refers to a capsule prepared from a mixture of gelatin and acrylic.

SUM04 [vi] JP59036540-A, which refers to microcapsules formed from gelatin and gun arabic, sodium alginate or **carrageenan** wherein the microcapsules are **coated** with flour, starch, powdered fat, **cellulose** protein, inorganic salt, organic acid salt, amino acid and sugar.

SUM04 . . . have been used for food coated capsules include sucrose, starch, talcum powder, hanno powder (liquorice powder), rubber, grape sugar, crystalline **cellulose**, lactose titanium dioxide, calcium carbonate, ammonium phthalate, **cellulose** and other associated **cellulose** derivatives, sorbitol, water and **polyvinyl** alcohol.

DETD . . . gelatin (block or powder form) in a container jacketed in hot water. The resultant mix is poured out onto an easy-**release** flat surface such as Teflon PP or PE and dried in a refrigerator. The resultant thin sheet is impervious to.

DETD (1) the use of seaweed makes a thin but exceedingly strong coating for a drug due to the fibrous or **cellulosic** value of the veins of seaweed leaves which are resistant to stomach acids such as dilute HCl but which readily.

DETD . . . of an alginate binder strongly resembles the alginate constituents of seaweed and thus the sealant soaks into the fibrous or **cellulosic** structure of the seaweed thereby facilitating strong bonding between seaweed pieces or shreds. A possible explanation for this is that.

DETD . . . the capsules are formed from natural products which are part of the normal Japanese diet thereby substantially eliminating approval from **pharmaceutical** regulatory authorities such as the *FDA;*

L57 ANSWER 51 OF 79 USPATFULL on STN
ACCESSION NUMBER: 1999:117022 USPATFULL
TITLE: Method of drug delivery and coated oral dosage forms for use in the method
INVENTOR(S): Yashiro, Shintaro, Kanagawa-ken, Japan
PATENT ASSIGNEE(S): Phillip Postey
n. Gunter Pauli, Kanagawa-ken, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5954956		19990928	<--
	WO 9617799		19960613	<--
APPLICATION INFO.:	US 1997-849767		19970606 (8)	<--
	WO 1995-AU921		19951206	<--
			19970606	PCT 371 date
			19970606	PCT 102(e) date

	NUMBER	DATE	
PRIORITY INFORMATION:	JP 1994-333235	19941205	<--
	AU 1995-3288	19950531	<--
	JP 1995-239933	19950914	<--
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Levy, Neil S.		
LEGAL REPRESENTATIVE:	Griffin, Butler, Whisenhunt & Szipl, LLP		
NUMBER OF CLAIMS:	19		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	6 Drawing Figure(s); 2 Drawing Page(s)		
LINE COUNT:	639		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A coating for a drug wherein said coating is formed from seaweed and/or kelp, the seaweed and/or kelp being of a type which is impervious to gastric acidity but denaturable by alkali found in the intestines. Suitably, the coating comprises a capsule which also incorporates a binder or the coating may comprise barium sulfate or other acid-resistant bulking agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AI	19951205	
	19970605	PCT 371 date
	19970605	PCT 102(e) date

SUM04 . . . inert polymers that control drug diffusion, polymers can be designed to dissolve, swell, or degrade in a controlled manner, thereby **releasing** the incorporated drug. It is, however, necessary that the polymer be transformed into a water-soluble product that evokes no limiting. . . . undergoes a phase change during which it or its by-products are removed or eliminated from the body, either during drug **release** or when most of the drug is deployed.
SUM04 The *polymers investigated* for such systems include polyesters,

L57 ANSWER 52 OF 79 USPATFULL on STN
ACCESSION NUMBER: 1999:102564 USPATFULL
TITLE: Durable hydrophilic coating for a porous hydrophobic polymer substrate
INVENTOR(S): Yablaoui, Ali, Roswell, GA, United States
Ning, Xin, Alpharetta, GA, United States
Bollas, II, Charles Edward, Buford, GA, United States
McDowall, Debra Jean, Roswell, GA, United States
Potts, David Charles, Dunwoody, GA, United States
Vankoot, Daniel Joseph, Roswell, GA, United States
PATENT ASSIGNEE(S): Kimberly-Clark Worldwide, Inc., Neenah, WI, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5945179		19990831	<--
APPLICATION INFO.:	US 1998-109678		19980702 (9)	<--
RELATED APPLN. INFO.:	Division of Ser. No. US 1996-631172, filed on 14 Jun 1996, now patented, Pat. No. US 5814567			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Cameron, Erma			
LEGAL REPRESENTATIVE:	Maycock, William E.			
NUMBER OF CLAIMS:	12			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	3 Drawing Figure(s); 3 Drawing Page(s)			
LINE COUNT:	3116			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A coated porous substrate composed of a hydrophobic polymer which is substantially uniformly coated with a hydrophilic polymeric material. The substrate may be a sheet-like material, examples of which are foams, fibers, and fibrous webs. The fibrous webs desirably will be nonwoven webs. The coating on the substrate is durable to an aqueous medium at a temperature in a range of from about 10° C. to about 50° C. and does not significantly suppress the surface tension of an aqueous medium with which the coated substrate may come in contact. The hydrophobic polymer may be a polyolefin, such as polyethylene or polypropylene. The hydrophilic polymeric material with which the polymer fibers are coated may be a polysaccharide or a modified polysaccharide. Also provided is a method of preparing a coated porous substrate which involves providing a porous substrate composed of a hydrophobic polymer. At least a portion of the substrate then is exposed to a field of reactive species. At least a portion of the porous substrate, including the portion exposed to the reactive species, is treated with a mixture which includes water and a hydrophilic polymeric material under conditions sufficient to substantially uniformly coat the porous substrate with the hydrophilic polymeric material.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM04 . . . groups also may be pendant groups. For example, the modified polysaccharide may be, by way of example only, a modified **cellulose**. For example, the hydrophobic groups may be pendant nonovalent alkyl groups, such as ethyl groups. As another example, the hydrophilic

L57 ANSWER 52 OF 79 USPATFULL on STN (Continued)
DETD . . . carrageenans, furcellaran, alginates, locust bean gum, gum arabic, guar gum, gum konjac, and gum karaya; microbial fermentation products, such as **gellan gum**, xanthan gum, and dextran gum; **cellulose**, such as microcrystalline **cellulose**; and animal products, such as hyaluronic acid, heparin, chitin, and chitosan.
DETD . . . may be adapted to render the polymeric material hydrophilic. By
way of illustration only, examples of modified polysaccharides include modified **celluloses** or **cellulose** derivatives, such as hydroxyethyl **cellulose**, hydroxypropyl **cellulose**, methyl **cellulose**, ethyl **cellulose**, methyl hydroxypropyl **cellulose**, ethyl hydroxyethyl **cellulose**, and carboxymethyl **cellulose**; starch and pectin derivatives, such as carboxymethyl starch, starch aldehyde, and pectinic and animal product derivatives, such as carboxymethyl chitin.
DETD . . .
DETD . . . Particularly useful types of polysaccharides and modified polysaccharides include, by way of illustration, agar; alginates; and modified **celluloses**, such as ethyl hydroxyethyl **cellulose**. In modified polysaccharides, particularly in the useful type of modified **cellulose**-coated fabric is durable to multiple exposures of 100 ml of water.
DETD . . . Example 1 was repeated, except that two other nonwoven fabrics,
Fabrics B and C, were utilized and another ethyl hydroxyethyl **cellulose** (EHEC60, Akzo Nobel), referred to hereinafter as Coating B, also was employed. Fabric B was a spunbond web composed of . . .
DETD . . . an aqueous solution containing 0.2 percent by weight of a Nalco
mixture by weight of agar (American Bio-organics Co.) and **carrageenan** (Kappa-**Carrageenan**, IWC Corporation) (**Coating** F). The fabric was completely saturated in the bath. The treated fabric exhibited vertical wicking heights of 15 cm and . . .
DETD . . . Example 5 was repeated, except that the fabric was dipped into an aqueous solution containing 0.3 percent by weight of **gellan gum** (Coating G, Gelrite®, Kelco Co.). The fabric was completely saturated in the bath. The treated fabric exhibited vertical wicking heights.
DETD Upon replacing the **gellan gun** solution with a 0.2 percent by weight solution of locust bean gum (Coating H, L8G, Aldrich Chemical Co.), the treated. . . .
DETD . . . . . a percentage of sample dry weight.
.sup.e Percent surface tension depression.

L57 ANSWER 52 OF 79 USPATFULL on STN (Continued)

Vertical Wicking Data for Each Nonwoven Web and A Laminate of both Webs, All Being Coated with Ethyl Hydroxyethyl **Cellulose**

Vertical Wicking Height (cm)			
Time (min)	Laminate	Fabric B	Fabric C
1.0	5.0	1.0	3.5
2.0	8.0	2.5	4.0
4.0	15.0	4.0	6.0

CLM What is claimed is:
7. The method of claim 6, which the modified polysaccharide is a modified **cellulose**.

IT 9000-07-1, Carrageenan 9000-40-2, Locust bean gun 9002-18-0, Agar 9004-58-4, Bermocoll E 491 9071-35-0, Calcium alginate 9012-36-6, Agarose 67021-66-0, Calcium polygalacturonate **71010-32-1**, **Gellan gum**
(coating; durable hydrophilic coating for a porous hydrophobic polymer substrate)
IT **71010-32-1**, **Gellan gum**
(coating; durable hydrophilic coating for a porous hydrophobic polymer substrate)

L57 ANSWER 52 OF 79 USPATFULL on STN (Continued)
.sup.c Fluorescent surface tension depression.
.sup.d Plasma.
.sup.e Agar.
.sup.f Agarose.
.sup.g Agar/carrageenan.
.sup.h **Gellan gum**.
DETD . . . . . gum) polypropylene meltblown fabric having a width of 14 inches
(about 36 cm) (Fabric C) was coated with ethyl hydroxyethyl **cellulose** (Coating A) as described in Example 1. The coated fabric then was oxidized in a one inch zone along the. . . .
DETD TABLE 6

Water Contact Angles for Polypropylene Films Coated with Ethyl Hydroxyethyl **Cellulose**	
Material	Contact Angle (°)
Control	97
Coated only (side zones)	30
Coated and corona treated (central zone)	0

DETD Table 8 demonstrates the improvements in wettability resulting from the coating of ethyl hydroxyethyl **cellulose**, and such coating combined with a post-corona treatment. The table also demonstrates the advantage in the post-corona treatment of the. . . .
DETD TABLE 9

XPS Data for Polypropylene Nonwoven Webs Coated with Ethyl Hydroxyethyl **Cellulose**	
Material	O/C Atom-Percent Ratio
Control	0.01
Coated only (side zones)	0.55
Coated and corona treated (central zone)	0.75

DETD TABLE 10

Vertical Wicking Data for Polypropylene Nonwoven Webs Coated with Ethyl Hydroxyethyl **Cellulose** With and Without a Post-RFGD Treatment

Time (min)	Vertical Wicking Height (cm) Central Zone	Side Zones
1.5	6.0	3.5
3.0	8.5	4.5
5.0	12.0	7.0
10.0. . .		
DETD TABLE 11

L57 ANSWER 53 OF 79 USPATFULL on STN
ACCESSION NUMBER: 1999:17431 USPATFULL
TITLE: Biodegradable laminated films fabricated from pectin and chitosan
INVENTOR(S): Hoagland, Peter D., Schenkaville, FA, United States
PATENT ASSIGNEE(S): The United States of America, as represented by the Secretary of Agriculture, Washington, DC, United States
(U.S. government)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5919574		19990706	<--
APPLICATION INFO.:	US 1995-580663		19951229 (8)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Timmerman, John J.			
ASSISTANT EXAMINER:	LaVilla, Michael			
LEGAL REPRESENTATIVE:	Silverstein, M. Howard, Fado, John D., Graeter, Janelle			
NUMBER OF CLAIMS:	5			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 6 Drawing Page(s)			
LINE COUNT:	633			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB High modulus, flexible laminated films may be fabricated from chitosan and pectin. Either glycerol or lactic acid as plasticizer and, optionally, starch may also be blended with either the pectin or chitosan solutions used for film preparation. The laminated films are biodegradable, and the components are derived from renewable agricultural products.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM The film-forming properties of several water soluble polysaccharides have been studied. Films useful for **coatings** made from alginates and **carrageenans** were disclosed by Rosetter et al. (Food Technology. 1986. vol. 12:(3), pp. 47-59). Paper coatings and similar applications of carboxymethyl **cellulose** and other **celluloses** others have been investigated, and studies of chitin and chitosan films, including self-supporting films, have also been carried out (Peniston, . . .
SUMM . . . involved derivatized pectins used with divalent cations such as
calcium. A more recent work discussed blends of pectins and carboxymethyl **cellulose** for use as cigarette papers (Lind et al., U.S. Pat. No. 4,129,134, 1978). U.S. Pat. No. 2,542,052 (issued to H . . .
SUMM Films from composites of chitosan and **cellulose** have been made by casting dispersions on steel or chrome plates at elevated temperatures from 70° to 100° C. (Nishyama, . . .
SUMM . . . (El Ghaouth et al. 1991. J. Food Process. Preserv. vol. 15, pp.
113-137). Chitosan films have been investigated for controlled release of **pharmaceuticals** (Bonvin and de Bertorella. 1993. Polym. Bull. (Berlin). vol. 31, pp. 375-379).
DETD . . . include chitosan for several reasons. First, chitosan is derived from chitin, the second most abundant polysaccharide on the earth, after **cellulose** (Lezica and Quesada-Allue. 1990. Methods in

L57 ANSWER 53 OF 79 USPATFULL on STN (Continued)
Plant Biochem. vol. 2, pp. 447-481, and is commercially available from a stable, renewable. . .

DETD . . . of the invention are useful for a number of applications including medicinal applications such as patches for the delivery of **pharmaceuticals** to skin; biodegradable, disposable pouches or bags for frozen or dried foods or soil additives; coatings for controlled **release**, adhesive bonding or protection; embedding and preserving agents for microscopic specimens; and encapsulation of living cells.

L57 ANSWER 54 OF 79 USPATFULL on STN
ACCESSION NUMBER: 1998:159374 USPATFULL
TITLE: Bioresorbable sealants for porous vascular grafts
INVENTOR(S): Lentz, David J., Randolph, NJ, United States
Loomis, Gary L., Morristown, NJ, United States
Moroni, Antonio, Morris Plains, NJ, United States
DeFreitas, Jennifer, Rockville Park, NJ, United States
PATENT ASSIGNEE(S): Meadox Medicals, Inc., Oakland, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5851229		1998122	<--
APPLICATION INFO.:	US 1996-713901	(8)	1996913	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Rittingthon, Debra S.			
LEGAL REPRESENTATIVE:	Hoffmann & Baron, LLP			
NUMBER OF CLAIMS:	19			
EXEMPLARY CLAIM:	1			
LINE COUNT:	1156			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A bioresorbable sealant composition useful for impregnating implantable soft-tissue prostheses includes at least two polysaccharides in combination to form a hydrogel or sol-gel. The sealant compositions may optionally include a bioactive agent and/or be cross-linked subsequent to application of these compositions to the substrate surface.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM01 . . . hydrogel or sol-gel mixtures of polysaccharides that render such grafts blood-tight. Another aspect of the invention is directed toward providing timed-**released** delivery of therapeutic agents impregnated within the interstitial spaces of such grafts. Methods of providing these grafts are also provided.

SUM01 In the present invention, useful polysaccharides include algin, carboxymethyl **cellulose**, carrageenan, including carrageenan type I, carrageenan type II, carrageenan type III, and carrageenan type IV, furcellaran, agarose, guar, locust bean gum, gum arabic, hydroxyethyl **cellulose**, hydroxypropyl **cellulose**, methyl **cellulose**, hydroxyalkylmethyl **cellulose**, pectin, partially de-acetylated chitosan, starch and starch derivatives including, amylose and amylopectin, xanthan, gasels, polyglycine, hyaluronic acid and its derivatives,

SUM01 The present invention also contemplates incorporating a therapeutic or bioactive agent into the hydrogel. In this way, the hydrogel controllably **releases** the therapeutic agent while the hydrogel is biodegraded or bioresorbed. One particularly useful class of therapeutic agents is the anticoagulants. . . for such purposes, but among those currently known as being useful are heparin, sulfated polysaccharides, prostaglandin, urokinase, hirudin streptokinase, their **pharmaceutical**

L57 ANSWER 54 OF 79 USPATFULL on STN (Continued)
salts and mixtures thereof. Heparin is preferred because it is a polysaccharide and is easily incorporated into a hydrogel. Furthermore,

SUM06 In another embodiment of the invention, a controlled **release** material is provided that includes a hydrogel matrix formed from at least two polysaccharides and an anticoagulant agent incorporated within. . .

SUM06 . . . aqueous medium form a hydrogel. This hydrogel forms a liquid-tight seal when applied to the prosthesis as a sealant. A controlled-**release**, bioresorbable sealant composition is also provided whereby in addition to the combination of at least two polysaccharides, there is also included a therapeutic or bioactive agent which is slowly **released** in the body subsequent to implantation as the sealant gradually biodegrades and tissue ingrowth increases.

SUM06 . . . used to define such sealant matrices. In particular, the following list of polysaccharides may be used herein: heparin, algin, carboxymethyl **cellulose**, carrageenan, including carrageenan type I, carrageenan type II, carrageenan type III, and carrageenan type IV; furcellaran, agarose, guar, locust bean gum, gum arabic, hydroxyethyl **cellulose**, hydroxypropyl **cellulose**, methyl **cellulose**, hydroxyalkylmethyl **cellulose**, pectin, chitosan; starch and starch derivatives including, amylose and amylopectin; xanthan, their salts, and mixtures thereof. Certain proteins and polyamino. . . proteins, locust bean

induces connective . . .
soluble, non gelling gum tissue growth
Chitosan Contains --NH2.sub.2 Hyaluronic acid, Stimulates
Heparin, Chondroitin macrophage
Sulfate, **Cellulose** growth, anti-
Sulfate, and Sodium infective agent,
Carboxymethyl to **carrageenan**
immuno-enhancer,
Cellulose hemostatic, accelerates wound
healing
Furcellaran
Polyanion, contains Locust bean gum, K.sup.+, properties similar
some SO.sub.3 H, fewer Ca.sup.+2, milk proteins
than the kappa
carrageenans but more than Agar; forms flexible, opalescent gels
Guar Gum Nonionic, disperses Borates, Xanthan
Viscosity increases
at . . polysaccharide, colloid action
highly soluble,

L57 ANSWER 54 OF 79 USPATFULL on STN (Continued)
forms Newtonian solutions with low viscosity, even at low concentrations
Hydroxyethyl
Nonionic, both Sodium carboxymethyl Properties not
Cellulose, form clear, smooth **cellulose** affected by pH,
Hydroxypropyl solutions and Newtonian at low
Cellulose impermeable films shear rates, pseudo plastic at high shear rates
Locust Bean Gum
Nonionic, partially kappa carrageenan,
soluble in. . . Viscosity increases forms pseudo
water, gels upon plastic solutions cooling
Sodium Polyanion, hydrates Casein, Soy Protein,
Carboxymethyl rapidly to form Guar Gum, HPC and
Cellulose clear solutions Chitosan
Xanthan Gun
Anionic, forms Locust Bean Gun
viscous, strongly Viscosity does not (thermally reversible change
pseudo plastic gel), Guar Gun significantly with
solutions (weak), Methyl temperature or pH
Cellulose

SUM08 . . . the sealant. In this way, as the sealant's polysaccharide matrix biodegrades the bioactive agent, i.e. anticoagulant agent, may be controllably **released** over time. Thus, the anticoagulant agent augments the sealant's ability to prevent blood leakage through, for example, the walls of. . . the present invention, the anticoagulant agent may be a prostaglandin, a urokinase, a streptokinase, a sulfated polysaccharide, an albumin, their **pharmaceutical** salts and mixtures thereof. Other suitable anticoagulant agents may also be used. Preferably, the anticoagulant agent is heparin or its **pharmaceutical** salt.

SUM08 In yet another embodiment of the present invention, an anticoagulant

L57 ANSWER 54 OF 79 USPATFULL on STN (Continued)
agent or other bioactive agent dispersed within a controlled **release** material is impregnated within the interstitial space between the inner and outer surfaces of a porous implantable device. The controlled **release** material is a hydrogel matrix containing at least two polysaccharides as described hereinabove. Thus, as the hydrogel is biodegraded by natural enzymes present in the body, the anticoagulant agent is slowly **released** over time. Accordingly, in addition to imparting a substantially blood-tight seal to, for example, a vascular graft, the hydrogel matrix as it biodegrades, also provides a support structure from which the anticoagulant or bioactive agent is controllably **released**. In this way, the controlled **release** of the anticoagulant enhances the ability of this hydrogel composition to prevent blood loss to the patient by coagulating any. . .
SUMM According to Kinam Park et al., Biodegradable Hydrogels For Drug Delivery (Technomic Publishing Co. 1993), drug **release** in a hydrogel system is influenced by various formulation variables such as physiochemical properties of the components in the system. Thus, in addition to polymer degradation, **release** of the anticoagulant is affected by the physical parameters of the polymer, such as, water content, degree of crosslinking, crystallinity, . . . aqueous medium and the amount of drug loaded into the hydrogel are also expected to have significant effects on the **release** characteristics of the drug-polymer composite. Accordingly, the **release** rate of the anticoagulant agent will vary according to the variables disclosed hereinabove. Providing the appropriate **release** rate, however, can be achieved by one skilled in the art by adjusting these parameters. . . .
SUMM . . . used in the present invention, including, for example, algin, starch amylose and its derivatives, carrageenan, including types I-IV, pectin, and **cellulose** derivatives. Similarly, the branched polysaccharides of the present invention are water-soluble polymers that
produce viscous aqueous dispersions. Thus, all members. .
DETD . . . 0.01
Knitted Double
0.8 24 2600 43.13
Velour 1*
Knitted Double
0.8 24 2650 47.96
Velour 2.sup.+
Knitted Double
0.8 21 1050 19.90
Velour 3.sup.#
Woven 0.8 **27** 2000 **29.49**
(**carrageenan**
type II alone)*
Woven 0.8 **28** 300 **4.27**
(**carrageenan**
type II alone).sup.#
*Graft impregnated with 23° C. sealant and dried at room temperature.
.sup.+ Graft impregnated with 60° C. sealant. . .
DETD . . . Both the woven and knitted grafts held more water when the sealant was injected at 60° C. The woven grafts **coated** with

L57 ANSWER 54 OF 79 USPATFULL on STN (Continued)
carrageenan type II alone were significantly more porous than grafts **coated** with the **carrageenan** type II/locust bean mixture. Drying the **carrageenan** type II **coated** graft at 60° C. significantly improved water tightness as demonstrated in the porosity tests. All grafts were soft and flexible.
DETD As Examples **1**-3 demonstrate, **carrageenan** types II and IV were more effective in sealing the grafts when used in combination with locust bean gum than. . . .
DETD The woven grafts **coated** with **carrageenan** type II alone did not pose comparable results to the woven grafts **coated** with the **carrageenan** type II and locust bean gum combination. The results in Table 4, however, demonstrate that the carrageenan type II impregnated grafts dried at 60° C. allowed more sealant to adhere to the graft and were less porous. Grafts **coated** with 60° C. 23° C. 0.27
-- IV/150 ml water 15 g 8 mm Room Temp Sealant 1.5 g. . .
CLM What is claimed is:
2. The prosthesis as in claim 1 wherein said polysaccharides are selected from the group consisting of algin, carrageenan, furcellaran, agarose, gar, locust bean gum, gum arabic, hydroxyethyl **cellulose**, hydroxypropyl **cellulose**, methyl **cellulose**, hydroxyalkylmethyl **cellulose**, pectin, partially deacetylated chitosan, starch and starch derivatives including, amylose and amylopectin, xanthan, casein, polylysine, hyaluronic acid and its derivatives,. .
CLM What is claimed is:
11. The prosthesis as in claim 1 wherein an anticoagulant agent is incorporated into said hydrogel, said hydrogel controllably **releasing** said anticoagulant through said porous walls.
CLM What is claimed is:
. . . 12. wherein said anticoagulant agent is selected from the group consisting of heparin, prostaglandin, urokinase, streptokinase, sulfated
polysaccharide, albumin, their **pharmaceutical** salts and mixtures thereof.
CLM What is claimed is:
15. A controlled-**release** bioresorbable sealant composition for use in soft tissue prostheses comprising: a hydrogel matrix, a bio-active agent
incorporated therein, said hydrogel. . .

L57 ANSWER 55 OF 79 USPATFULL on STN
ACCESSION NUMBER: 1998:113987 USPATFULL
TITLE: Durable hydrophilic coating for a porous hydrophobic substrate
INVENTOR(S): Yahiaoui, Ali, Roswell, GA, United States
Ning, Xin, Alpharetta, GA, United States
Bolian, II, Charles Edward, Buford, GA, United States
McDowall, Debra Jean, Roswell, GA, United States
Potts, David Charles, Dunwoody, GA, United States
Vandiver, Daniel Joseph, Roswell, GA, United States
PATENT ASSIGNEE(S): Kimberly-Clark Worldwide, Inc., Neenah, WI, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5814567		19980929	<--
APPLICATION INFO.:	US 1996-665172		19960614 (8)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Bell, James J.			
LEGAL REPRESENTATIVE:	Maycock, William E.			
NUMBER OF CLAIMS:	15			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	3 Drawing Figure(s); 3 Drawing Page(s)			
LINE COUNT:	3109			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A coated porous substrate composed of a hydrophobic polymer which is substantially uniformly coated with a hydrophilic polymeric material. The substrate may be a sheet-like material, examples of which are foams,
fibers, and fibrous webs. The fibrous webs desirably will be nonwoven webs. The coating on the substrate is durable to an aqueous medium at a temperature in a range of from about 10° C. to about 50° C. and does not significantly suppress the surface tension of an aqueous
medium with which the coated substrate may come in contact. The hydrophobic polymer may be a polyolefin, such as polyethylene or polypropylene. The hydrophilic polymeric material with which the polymer
fibers are coated may be a polysaccharide or a modified polysaccharide. Also provided is a method of preparing a coated porous substrate which involves providing a porous substrate composed of a hydrophobic polymer.
At least a portion of the substrate then is exposed to a field of reactive species. At least a portion of the porous substrate, including the portion exposed to the reactive species, is treated with a mixture which includes water and a hydrophilic polymeric material under conditions sufficient to substantially uniformly coat the porous substrate with the hydrophilic polymeric material.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . groups also may be pendant groups. For example, the modified polysaccharide may be, by way of example only, a modified **cellulose**. For example, the hydrophobic groups may be pendant nonvolent alkyl groups, such as ethyl groups. As another example, the hydrophilic. .
DETD . . . carrageenans, furcelleran, alginates, locust bean gum, gum

L57 ANSWER 55 OF 79 USPATFULL on STN (Continued)
arabic, ghat gum, gum karaya, and gum karaya; microbial fermentation products, such as **gellan gum**, xanthan gum, and dextran gum; **cellulose**, such as microcrystalline **cellulose**; and animal products, such as hyaluronic acid, heparin, chitin, and chitosan.
DETD . . . may be adapted to render the polyvenic material hydrophilic.
By
way of illustration only, examples of modified polysaccharides include modified **cellulose** or **cellulose** derivatives, such as hydroxyethyl **cellulose**, hydroxypropyl **cellulose**, methyl **cellulose**, ethyl **cellulose**, methyl hydroxypropyl **cellulose**, ethyl hydroxyethyl **cellulose**, and carboxymethyl **cellulose**; starch and pectin derivatives, such as carboxymethyl starch, aldehyde, and pectate; and animal product derivatives, such as carboxymethyl chitin.
.
DETD Particularly useful types of polysaccharides and modified polysaccharides include, by way of illustration, sugar; alginates; and modified **celluloses**, such as ethyl hydroxyethyl **cellulose**. In modified polysaccharides, particularly in the useful type of modified polysaccharides just noted, the hydrophobic groups may be pendant heavenlast. . .
DETD . . . Immediately following the corona treatment, the fabric was dipped in a 0.25 percent by weight aqueous solution of ethyl hydroxyethyl **cellulose** (Bermocol E481, Akzo Nobel), referred to hereinafter as Coating A. After complete saturation of the fabric, indicated by a change. . .
DETD . . . the fabric. An Instantaneous absorption was observed which indicated that the fabric was substantially uniformly coated with the ethyl hydroxyethyl **cellulose** (Coating A).
DETD . . . y-axis), respectively, versus wash cycle number. The plot is shown as FIG. 1. The figure clearly indicates that ethyl hydroxyethyl **cellulose**-coated fabric is durable to multiple exposures of 100 ml of water.
DETD . . . Example 1 was repeated, except that two other nonwoven fabrics,
Fabrazz B and C, were utilized and another ethyl hydroxyethyl **cellulose** (BERMOL, Akzo Nobel), referred to hereinafter as Coating B, also was employed. Fabric B was a spunbond web composed of . . .
DETD . . . an aqueous solution containing 0.2 percent by weight of a 90:10
mixture by weight of agar (American Bio-organics Co.) and **carrageenan** (Kappa-**Carrageenan**, FMC Corporation) (**Coating F**). The fabric was completely saturated in the bath. The treated fabric exhibited vertical wicking heights of 13 cm and. . .
DETD . . . Example 3 was repeated, except that the fabric was dipped into an aqueous solution containing 0.3 percent by weight of **gellan gum** (Coating G, Gelrite®, Neiva Co.). The fabric was completely saturated in the bath. The treated fabric exhibited vertical wicking heights. . .
DETD Upon replacing the **gellan gum** solution with a 0.2 percent by weight solution of locust bean gum (Coating H, LBG, Aldrich Chemical Co.), the treated. . . .
DETD . . . Expressed as a percentage of sample dry weight.
.sup.c Percent surface tension depression.
.sup.d Plasma.

L57 ANSWER 55 OF 79 USPATFULL on STN (Continued)
.sup.e Agar.
.sup.g Agar/carrageenan.
.sup.h **Gellan gum**.
DETD . . . gum) polypropylene meltblown fabric having a width of 14 inches
(about 36 cm) (Fabric C) was coated with ethyl hydroxyethyl **cellulose** (Coating A) as described in Example 1. The coated fabric then was oxidized in a one inch zone along the. . . .
DETD TABLE 8

Water Contact Angles for Polypropylene Films
Coated with Ethyl Hydroxyethyl **Cellulose**

Material	Contact Angle (°)
Control 1	97
Coated only (side zones)	30
Coated and corona treated (central zone)	0

DETD Table 8 demonstrates the improvements in wettability resulting from the coating of ethyl hydroxyethyl **cellulose**, and such coating combined with a post-corona treatment. The table also demonstrates the advantage in the post-corona treatment of the. . . .
DETD TABLE 9

XPS Data for Polypropylene Nonwoven Webs
Coated with Ethyl Hydroxyethyl **Cellulose**

Material	O/C Atom-Percent Ratio
Control	0.01
Coated only (side zones)	0.55
Coated and corona treated (central zone)	0.75

DETD TABLE 10

Vertical Wicking Data for Polypropylene Nonwoven Webs Coated with Ethyl Hydroxyethyl **Cellulose** With and Without a Post-RFGD Treatment

Time (min)	Vertical Wicking Height (cm) Central Zone	Side Zones
1.5	6.0	3.5
3.0	8.5	4.5
5.0	12.0	7.0
10.0. . .		

DETD TABLE 11

Vertical Wicking Data for Each Nonwoven Web

L57 ANSWER 56 OF 79 USPATFULL on STN
ACCESSION NUMBER: 1998:157750 USPATFULL
TITLE: Capsule shell
INVENTOR(S): Yasaeng, Tuta, Osaka, Japan
Matsuura, Seinosuke, Souraku-gun, Japan
Akai, Kazuhiro, Kashihara, Japan
PATENT ASSIGNEE(S): Japan Elanco Co., Ltd., Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5756123		19980526	<--
APPLICATION INFO.:	US 1997-797622		19970207 (8)	<--
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-548285, filed on 25 Oct 1995, now abandoned			

	NUMBER	DATE	
PRIORITY INFORMATION:	JP 1994-323581	19941201	<--
	JP 1994-333965	19941216	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Helina, Amy
LEGAL REPRESENTATIVE: Birch, Stewart, Kolasch & Birch, LLP
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 586
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A capsule shell comprising 79.6-98.7% by weight of a hydroxypropylmethyl
cellulose, 0.03-0.5% by weight of **carrageenan**, and 0.14-3.19% by weight of a potassium ion and/or a calcium is prepared by drying an solution comprising 18-28% by weight of hydroxypropylmethyl **cellulose** whose 2% aqueous solution has a viscosity of 2.4-5.4 centistokes at 20° C. as a base, 0.01-0.09% by weight of carrageenan as a gelling agent, and 0.05-0.6% by weight of a potassium ion and/or calcium
ion as a co-gelling agent. The capsule shell exhibits disintegrating ability equivalent to gelatin shells without degrading that ability even
under special conditions containing much calcium ions.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A capsule shell comprising 79.6-98.7% by weight of a hydroxypropylmethyl
cellulose, 0.03-0.5% by weight of **carrageenan**, and 0.14-3.19% by weight of a potassium ion and/or a calcium is prepared by drying an solution comprising 18-28% by weight of hydroxypropylmethyl **cellulose** whose 2% aqueous solution has a viscosity of 2.4-5.4 centistokes at 20° C. as a base, 0.01-0.09% by weight of. . . .
SUMM . . . to a capsule shell for forming medical hard capsules. More particularly, it relates to such a capsule shell using hydroxypropylmethyl **cellulose** as a base.
SUMM Medical capsules using a base other than gelatin are known in the art.

L57 ANSWER 56 OF 79 USPATFULL on STN (Continued)
Typically, capsules based on water- soluble **cellulose** derivatives were proposed. For example, Japanese Patent Publication (JP-B) No. 4310/1972 discloses a method for preparing capsules based on water-soluble **cellulose** ether from an aqueous solution of water-soluble **cellulose** ether. Japanese Patent Application Kokai (JP-A) Nos. 100519/1996 and 266660/1987 disclosea to prepare capsules from an aqueous solution of water-soluble **cellulose** ether and **polyvinyl** alcohol (PVA) blended therewith.

SUM4 The former shell-forming method involves the steps of immersing molding pins in an aqueous solution of water-soluble **cellulose** derivative and heating the pins and hence, the coating adhered thereto for gelation. The coating is not dried or solidified. . . . The heating temperature is too high. In the latter method of preparing capsules from

an aqueous solution of water-soluble **cellulose** derivative and PVA, the water-soluble **cellulose** derivative is subjected to the molding pins to gelled by immersing it in hot water. Some of the gelled coating can. .

SUM4 Additionally, these methods require a special apparatus or operation of heating the molding pins or immersing the molding pins with **cellulose** coating in hot water. Unfortunately, it is impossible to utilize the current manufacturing apparatus for gelatin capsules without a substantial. . .

SUM4 . . . , a medicol hard capsule having a low water content which is shaped from a capsule shell composition comprising a water-soluble **cellulose** derivative as a base, a gelling agent and a co-gelling agent. This capsule has equivalent performance to conventional gelatin capsules. . . .

SUM4 . . . . im solubility or disintegrating ability under certain conditions. More particularly, one preferable formulation of this capsule

shell composition uses hydroxypropylmethyl **cellulose** as a water-soluble **cellulose** derivative base, carrageenan as a gelling agent and a potassium ion as a co-gelling agent. Shell of this preferred formulation. . . containing much calcium ions, for example,

milk, then the capsule is retarded from disintegration. Then the drugs are not fully **released** or absorbed within a proper time, failing to fully exert their **pharmaceutical** effect. Therefore, it is desired to further improve the properties of the capsule based on a water-soluble **cellulose** derivative.

SUM4 An object of the present invention is to provide a capsule shell based on a water-soluble **cellulose** derivative which does not degrade its disintegration ability under special conditions where much calcium ions are present, that is, exerts.

SUM4 In connection with the capsule shell composition comprising hydroxypropylmethyl **cellulose** (to be abbreviated as HPMC, hereinafter) as a water-soluble **cellulose** derivative base, carrageenan as a gelling agent, and a potassium ion as a co-gelling agent wherein the shapability of HPMC. . .

SUM4 . . . to form a capsule shell comprising 79.6 to 98.7% by weight of the HPMC, 0.02 to 0.5% by weight of **carrageenan**, and 0.**1**4 to 3.3**9**% by weight of a co-gelling agent, there is obtained a capsule shell which

L57 ANSWER 56 OF 79 USPATFULL on STN (Continued)
Titanium oxide 0.77% 0.62%

Capsule shell
HPMC 90.63% 89.83%
κ- carrageenan 0.36% **1.12**%
Potassium chloride 0.50% 0.56%
(potassium ion) (0.26%) (0.29%)
Titanium oxide 3.51% 3.49%
Water 5**%** 5**%**

DETD . . . potassium chloride at 37° C. The opening time was measured by means of a disintegration tester as prescribed in the **Pharmacopoeia** of Japan. Three measurements were taken and an average was 15 calevlated. The results are shown in Table 2. As .

DETD . . . in milk at 37° C. The opening time was measured by meas of a disintegration tester as prescribed in the **Pharmacopoeia** of Japan. Three measurements were taken and an average was calculated. The results are shown in Table 3. As a. .

DETD . . . l and a conventional gelatin capsule were evaluated for disintegration ability in the first and second fluids prescribed in the **Pharmacopoeia** of Japan, Section 12. The capsules each were filled with 300 mg of a mixture of 20 parts by weight. .

DETD . . . equivalent disintegration ability to that of the conventional gelatin capsule in both the first and second fluids prescribed in the **Pharmacopoeia** of Japan. This suggests that the hard capsules of the shell according to the invention are useful as medical capsules. . .

DETD . . . pure water at about 75° C. With stirring, **κ**-carrageenan was added to the solution and dissolved therein. With stirring, hydroxypropylmethyl **cellulose** (HPMC) was added to the solution and dispersed therein. The solution was cooled to a temperature of 50° C. and. .

DETD . . . in milk at 37° C. The disselving time was measured by means of a disintegration tester as prescribed in the **Pharmacopoeia** of Japan. Three measurements were taken and an average was calculated. The results are shown in Table 5. As a. . . ion)

(0.5%)
(0.06%)
(0.06%)
(0.06%)
(0.05%)
(0.05%)
(0.05%)
(0.05%)
(0.05%)

Capsule shell
HPMC 95.55%
99.33%
99.07%
97.97%
97.18%
97.18%
97.18%

L57 ANSWER 56 OF 79 USPATFULL on STN (Continued)
maintains satisfactory disintegration ability even in the presence of calcium ions and exerts performance equivalent to conventional gelatin capsules. A hard capsule for **pharmaceutical** drugs of the capsule shell can be securely and efficiently produced according to the conventional immersion molding.

SUM5 Accordingly, the present invention provides a capsule shell comprising 79.6 to 98.7% by weight of a hydroxypropyl-methyl **cellulose**, 0.03 to 0.5% by weight of **carrageenan**, and 0.**14** to 3.3**9**% by weight of a potassium ion and/or a calcium ion, said capsule shell being prepared by

drying an aqueous solution comprising 10 to 20% by weight of hydroxypropyl-methyl **cellulose** having a viscosity of 2.4 to 5.4 centistokes as measured in a 2% aqueous solution at 20° C. as a. . .

DRWD . . . capsule of Example 1 and a conventional gelatin capsule when they were immersed in the first solution prescribed in the **Pharmacopoeia** of Japan.

DRWD . . . capsule of Example 1 and a conventional gelatin capsule when they were immersed in the second solution prescribed in the **Pharmacopoeia** of Japan.

DETD . . . weight in ionic amount. If the amount of co-gelling blended is less than 0.05% by weight, no satisfactory gelation of **carrageenan** is achieved and **shells** of sufficient gage cannot be formed by the dipping technique. If the amount of co-gelling agent blended exceeds 0.4% by. .

DETD . . . carrageenan as the gelling agent with the co-gelling agent. The

gelation of carrageenan follows the mechanism schematically shown in FIG. **1** that **carrageenan** molecules form double helix structures with the aid of the co-gelling agent (FIG. 1**B**) to form a three-dimensional network. If. . .

DETD . . . With stirring, **κ**-carrageenan and a coloring agent (titanium oxide) were added to the solution and dissolved therein. With stirring, hydroxypropylmethyl **cellulose** (HPMC) was added to the solution and dispersed therein. The solution was cooled to a temperature of 50° C. and.

DETD . . . Example 1
Example 1

Immersion solution

HPMC	7C-5S	--	16%
	7C-5MW	10%	--
	7C-5EW	10%	--
Viscosity		3.0 cst	
		6.0 cst	
κ- carrageenan		0.08%	**0.2**%
Potassium chloride		0.1**%**	0.3**%**
(potassium ion)		(0.06%)	(0.05%)

L57 ANSWER 56 OF 79 USPATFULL on STN (Continued)
98.0**1**%
96.**12**%
K-carrageenan
0.03%
0.**2**4%
0.40%
0.44%
1.22%
1.22%
1.22%
0.59%
1.92%
Potassium chloride
3.42%
0.43%
0.53%
0.59%
0.60%
0.60%
0.60%
0.40%
0.96%
(potassium ion)

DETD . . . With stirring, **κ**-carrageenan and a coloring agent (titanium oxide) were added to the solution and dissolved therein. With stirring, hydroxypropylmethyl **cellulose** (HPMC) having a viscosity of 5.87 centistokes as measured in a 2% aqueous solution at 20° C. was added to.

CLM What is claimed is:
1. A capsule shell comprising 79.6 to 98.7% by weight of a hydroxypropylmethyl **cellulose**, 0.03 to 0.5% by weight of **carrageenan**, and 0.**14** to 3.3**9**% by weight of a potassium ion and/or a calcium ion, said capsule shell being prepared by drying an aqueous solution comprising 10 to 20% by weight of hydroxypropyl-methyl **cellulose** having a viscosity of 2.4 to 5.4 centistokes as measured in a 2% aqueous solution at 20° C. as a. . .

CLM What is claimed is:
3. The capsule **shell** of claim 1 wherein said **carrageenan** gelling agent is κ-carrageenan and the co-gelling agent is a potassium ion.

CLM What is claimed is:
4. The capsule shell of claim 1 wherein the viscosity of the hydroxypropylmethyl **cellulose** is 3.0 to 4.6 centistokes as measured in a 2% aqueous solution at 20° C.

CLM What is claimed is:
6. A capsule shell comprising 79.8 to 98.7% by weight of a hydroxypropylmethyl **cellulose**, 0.14 to 0.3**%** by weight of **carrageenan**, and 0.**17** to 0.5% by weight of a potassium ion and/or a calcium ion, said capsule shell being prepared by drying an aqueous solution comprising 19 to 25% by weight of hydroxypropyl-methyl **cellulose** having a viscosity of 2.4 to 5.4 centistokes as measured in a 2% aqueous solution at 20° C. as a. . .

L57 ANSWER 57 OF 79 USPATFULL on STN
ACCESSION NUMBER: 87:93264 USPATFULL
TITLE: Films fabricated from mixtures of pectin and poly(vinyl alcohol)
INVENTOR(S): Coffin, David R., Glenside, PA, United States
Fishman, Marshall L., Lansdale, PA, United States
PATENT ASSIGNEE(S): The United States of America as represented by the Secretary of Agriculture, Washington, D.C, United States (U.S. government)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4646296		19870708	<--
APPLICATION INFO.:	US 1985-529299		19850918 (6)	<--
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1983-51431, filed on 23 Apr 1983, now patented, Pat. No. US 5451673			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Nutter, Nathan M.			
LEGAL REPRESENTATIVE:	Silverstein, M. Howard, Fado, John, Graeter, Janelle S.			
NUMBER OF CLAIMS:	19			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 8 Drawing Page(s)			
LINE COUNT:	662			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB High modulus, flexible films may be fabricated from blend of pectin, poly(vinyl alcohol) and, optionally, plasticizers. The combination of pectin and poly(vinyl alcohol) is advantageous in that pectin increases the biodegradability of poly(vinyl alcohol). In addition, the use of pectin provides effective utilization of an agricultural product.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . scientific and commercial interest. These films are not only biodegradable but may also be recyclable as well as acceptable for **pharmaceutical** applications. Multiple uses, ease of disposal and the replacement of petroleum-based raw materials with renewable agricultural products make these types. . .

SUMM The film-forming properties of several water soluble polysaccharides have been studied. Films useful for **coatings** made from alginates and **carrageenate** were disclosed by Kester et al. Food Technology, vol. 12 [1], pp. 47-59, (1986). Papers coatings and similar applications of carboxyethyl **cellulose** and other **cellulose** ethers have been investigated, and studies of chitin and chitosan films, including self-supporting films, have also been carried out (Averback, . . .

SUMM . . . involved derivatized pectins used with divalent cations such as calcium. A more recent work discussed blends of pectins and carboxyethyl **cellulose** for use as cigarette papers (Rind et al., U.S. Pat. No. 4,129,134, 1978). U.S. Pat. No. 2,542,052 (issued to H.B. .

L57 ANSWER 58 OF 79 USPATFULL on STN
ACCESSION NUMBER: 97127048 USPATFULL
TITLE: Method for amplification of nucleic acids in solid media
INVENTOR(S): Chetverin, Alexander B., Moskovskaya oblast, Puschino, nikrorajon AB, 24, 239, Russian Federation
Chetverina, Helena V., Moskovskaya oblast, Puschino, nikrorajon AB, 24, 239, Russian Federation

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5616479		19970401	<--
APPLICATION INFO.:	US 1992-966713		19921026 (7)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Caldwell, Stephanie W.			
ASSISTANT EXAMINER:	Campbell, Eggerton			
LEGAL REPRESENTATIVE:	Bond, William J.			
NUMBER OF CLAIMS:	38			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	10 Drawing Figure(s); 4 Drawing Page(s)			
LINE COUNT:	1627			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Amplification and/or expression of nucleic acids is carried out in a medium immobilized by using an organic and/or inorganic solid matrix penetrating the medium having a porous, fibrous, reticulated, coiled, capillary, lamellar or folded texture and which includes the components of a cell-free enzyme system of exponential amplification of nucleic acids and/or components of a cell-free enzyme system of nucleic acid expression. In this method, the products of each reaction cycle and the expression products remain in the same zone of the reaction volume where the matrix molecule was initially located. The method permits cloning of nucleic acids in vitro as well as detection of solitary nucleic acid molecules in the sample studied.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . or cell immobilization, as well as for growing bacteria, cells and viruses; such as agarose, polyacrylamide, nylon, gelatin, alginate, carrageenan, **cellulose**, silica gel, titanium sponge, cross-linked agarose, dextran or polyethylene glycol, and their combinations and derivatives are suitable (Primrose, S. B., . . . example, temperature-resistant media should be used to carry out PCR. In this case, matrices such as agarose, polyacrylamide, **cellulose**, polyamide (nylon), or of cross-linked agarose, dextran or polyethylene glycol, are appropriate.

DETD . . . the medium is immobilized, or having the reaction substrate(s) in a chemically unavailable "caged" form, which can be decomposed to **release** the normal substrate(s). An example of caged substrate as a photosensitive derivative of ATP, wherein the γ-phosphate is modified with a 1-(2-nitro)phenylethyl group (Kaplan, J. H., Forbush, B., III, and Hoffman, J. F. (1978). Rapid Photolytic **Release** of Adenosine 5'-Triphosphate from a Protected Analogue: Utilization by the Na:K Pump of Human Red Blood Cell Ghosts. Biochemistry 17, . . .

DETD . . . with polyethylene imine. Socks, C. (1987). Cell Immobilization in Calcium Alginate. Methods Enzymol. 135, 175-189. The granules can also be **coated** with lappa-**carrageenan** [Chibata, I., Tosa, T., Sato, T. and Takata, I. (1987). Immobilization of Cells in **Carrageenan**.

L57 ANSWER 57 OF 79 USPATFULL on STN (Continued)

DETD . . . adhesives, water-soluble pouches for dispensing pre-measured or hazardous substances, bags for washing linens of hospital patients with infectious diseases. Controlled **release** matrices, carriers or coatings which are water soluble also have numerous applications such as the application of **pharmaceutical** preparations to the skin. Biodegradable materials which are carrier matrices such as tablets or encapsulation materials are also contemplated.

DETD . . . weight were made by dissolving the polymers in water using the method recommended by Air Products Co. (Air Products, AIRVOL® **Polyvinyl** Alcohol product brochure, Allentown, Pa. 1990, herein incorporated by reference). This involved dispersing the polymer in cold water and then. . .

L57 ANSWER 58 OF 79 USPATFULL on STN (Continued)

Methods Enzymol. **135**, **189**-198), or with **cellulose** nitrate, nylon, and other types of semipermeable membranes [Chang, T. M. S. (1976). Microencapsulation of Enzymes and Biologicals. Methods Enzymol. . . .

DETD Fibrous thin layers, such as those based on **cellulose** or nylon, or porous layer such as based on silica gel or titanium sponge, are easy to prepare by soaking . . .

DETD . . . dextrans with epichlorohydrine or with N,N'-methylene bisacrylamide [Flodin, P. (1962). Dextran Gels and Their Applications in Gel Filtration, Dissertation, AB **Pharmacia**, Uppsala, Sweden; Osterman (1986), supra]. However, in most cases cross-linking occurs under conditions that cannot be tolerated by the enzymes. . .

DETD . . . is treated with 3M guanidine isothiocyanate solution, that results in the lysis of cells, denaturing of proteins (including nucleases), and **release** from cellular debris and denaturation of RNA and DNA [Pellegrino, M. G., Lewin, M. Meyer, W. A., III, Lanzisetti, R. . . . Employing dT-tailed Capture Probes. I. Multiple Capture Methods. Anal. Biochem. 181, 345-359]. After washing the beads, the target molecules are **released** into solution by heating in a low-salt buffer and used as templates for generation of a replicatable reporter from binary. . .

DETD . . . DNA targets. The extended sequence includes a copy of the target region (dashed line). The extended first probe is then **released** from the target, permitting its hybridization to a second probe (middle diagram) that contains the second probe sequence and a . . .

DETD . . . D. C. (1983). Rapid and Sensitive Colorimetric Method for Visualizing Biotin-labeled DNA Probes Hybridized to DNA or RNA immobilized on **Nitrocellulose**:Bio-blots. Proc. Natl. Acad. Sci. U.S.A. 80, 4045-4049]. Gene encoding phosphoprotein such as apo-osmlin (from hydroid Obelia geniculata) can be detected. . . .

CLM What is claimed is:
. . . to claim 1 wherein said solid matrix is selected from the group consisting of agarose, polyacrylamide, nylon, gelatin, alginate, carrageenan, **cellulose**, silica gel, titanium sponge, dextran, and polyethylene glycol.

CLM What is claimed is:
. . . said amplification system nucleic acid molecules, at least one of which may comprise a template for said amplification system; (d) **releasing** said at least one caged nucleotide; and (e) incubating said matrix layer containing said distribution molecules under conditions promoting synthesis. . .

L57 ANSWER 59 OF 79 USPATFULL on STN
ACCESSION NUMBER: 97:12854 USPATFULL
TITLE: Absorbent phycocolloids and a method for their manufacture
INVENTOR(S): Gross, James R., Appleton, WI, United States
PATENT ASSIGNEE(S): Kimberly-Clark Corporation, Neenah, WI, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5612411		19970318	<--
APPLICATION INFO.:	US 1992-977459		19921118 (7)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Mullis, Jeffrey			
LEGAL REPRESENTATIVE:	Mielke, Thomas J.			
NUMBER OF CLAIMS:	14			
EXEMPLARY CLAIM:	1			
LINE COUNT:	702			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described is a method for preparing a water-swellable, substantially water-insoluble material. The method involves forming a first solution containing a water-soluble phycocolloid. The first solution is then added to a second solution containing an ion capable of rendering the water-soluble phycocolloid substantially water insoluble. The phycocolloid material is then removed from the second solution and subjected to a solvent exchange to remove water present in the phycocolloid material. Hollow particles can be formed by including a gelation-retarding agent in the first solution. Also described is a water-swellable, substantially water-insoluble particle defining an interior void. The particle comprises an outer shell formed from a water-insoluble phycocolloid. The outer shell defines an interior void which contains a phycocolloid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM . . . an outer shell comprising a water-swellable, substantially water-insoluble phycocolloid. The phycocolloid is selected from the group consisting of algin and **carrageenan**. The outer **shell** defines an interior void. The interior void contains a phycocolloid.

SUM . . . other suitable water-soluble polysaccharides which may be included in the first solution include polysaccharide ethers such as carboxymethyl starch, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, methyl **cellulose** and the like; and guar gum, **gellan gum**, locust bean gum, xanthan gun and the like. In one preferred embodiment, the first solution comprises a combination of a . . . selected from the group consisting of algin and carrageenan and a water-soluble polysaccharide selected from the group consisting of carboxymethyl **cellulose**, carboxymethyl starch and guar gum. Examples of water-soluble synthetic polymers which may be included in the first solution include **polyvinyl** alcohol, **polyvinyl** pyrrolidone, poly(acrylic acid), poly(hydroxyethyl acrylate) and the like.

SUM . . . The particle comprises an outer shell comprising a water-swellable, substantially water-insoluble phycocolloid selected

L57 ANSWER 59 OF 79 USPATFULL on STN (Continued)
from the group consisting of algin and **carrageenan**. The outer **shell** defines an interior void. The interior void defined by the outer shell contains a phycocolloid. The phycocolloid is water swellable, . . .

DETD . . . weight percent, based on total weight of the first solution, of

a mixture of Na Alginate or carrageenan with carboxymethyl **cellulose** (CMC), commercially available from Aqualon under the trade designation **Cellulose** Gum Type 7HCF, carboxymethyl starch (CMS), commercially available from A. E. Staley Mfg. Co. under the trade designation

CS-450,

guar.

DETD . . . particles according to the present invention. For example, with

reference to Samples 37-42 and 44-49, Applicant notes that neither carboxymethyl **cellulose** nor carboxymethyl starch form absorbent particles according to the method of the present invention. However, when the carboxymethyl **cellulose** and carboxymethyl starch are combined with an algin or carrageenan, absorbent particles according to the present invention are formed through. . .

L57 ANSWER 60 OF 79 USPATFULL on STN
ACCESSION NUMBER: 96:84985 USPATFULL
TITLE: Absorbent phycocolloids and a method for their manufacture
INVENTOR(S): Gross, James R., Appleton, WI, United States
PATENT ASSIGNEE(S): Kimberly-Clark Corporation, Neenah, WI, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5556793		19960917	<--
APPLICATION INFO.:	US 1995-448062		19950523 (8)	<--
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1992-977459, filed on 18 Nov 1992			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Mullis, Jeffrey			
LEGAL REPRESENTATIVE:	Mielke, Thomas J.			
NUMBER OF CLAIMS:	4			
EXEMPLARY CLAIM:	2			
LINE COUNT:	673			

AB Described is a method for preparing a water-swellable, substantially water-insoluble material. The method involves forming a first solution containing a water-soluble phycocolloid. The first solution is then added to a second solution containing an ion capable of rendering the water-soluble phycocolloid substantially water insoluble. The phycocolloid material is then removed from the second solution and subjected to a solvent exchange to remove water present in the phycocolloid material. Hollow particles can be formed by including a gelation-retarding agent in the first solution. Also described is a water-swellable, substantially water-insoluble particle defining an interior void. The particle comprises an outer shell formed from a water-insoluble phycocolloid. The outer shell defines an interior void which contains a phycocolloid.

SUM . . . an outer shell comprising a water-swellable, substantially water-insoluble phycocolloid. The phycocolloid is selected from the group consisting of algin and **carrageenan**. The outer **shell** defines an interior void. The interior void contains a phycocolloid.

SUM . . . other suitable water-soluble polysaccharides which may be included in the first solution include polysaccharide ethers such as carboxymethyl starch, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, methyl **cellulose** and the like; and guar gum, **gellan gum**, locust bean gum, xanthan gun and the like. In one preferred embodiment, the first solution comprises a combination of a . . . selected from the group consisting of algin and carrageenan and a water-soluble polysaccharide selected from the group consisting of carboxymethyl **cellulose**, carboxymethyl starch and guar gum. Examples of water-soluble synthetic polymers which may be included in the first solution include **polyvinyl** alcohol, **polyvinyl** pyrrolidone, poly(acrylic acid), poly(hydroxyethyl acrylate) and the like.

SUM . . . The particle comprises an outer shell comprising a water-swellable, substantially water-insoluble phycocolloid selected from the group consisting of algin and **carrageenan**. The outer **shell** defines an interior void. The interior void defined by the outer shell contains a phycocolloid. The phycocolloid is water swellable, . . .

DETD . . . weight percent, based on total weight of the first solution, of

L57 ANSWER 60 OF 79 USPATFULL on STN (Continued)
a mixture of Na Alginate or carrageenan with carboxymethyl **cellulose** (CMC), commercially available from Aqualon under the trade designation **Cellulose** Gum Type 7HCF, carboxymethyl starch (CMS), commercially available from A. E. Staley Mfg. Co. under the trade designation

CS-450,

guar.

DETD . . . particles according to the present invention. For example, with

reference to Samples 37-42 and 44-49, Applicant notes that neither carboxymethyl **cellulose** nor carboxymethyl starch form absorbent particles according to the method of the present invention. However, when the carboxymethyl **cellulose** and carboxymethyl starch are combined with an algin or carrageenan, absorbent particles according to the present invention are formed through. . .

L57 ANSWER 61 OF 79 USPATFULL on STN
ACCESSION NUMBER: 95:102458 USPATFULL
TITLE: Methods of normalizing metabolic parameters in diabetics
INVENTOR(S): Phillips, William T., San Antonio, TX, United States
Schwartz, Joyce G., San Antonio, TX, United States
Greer, Gary M., San Antonio, TX, United States
PATENT ASSIGNEE(S): Board of Regents, The University of Texas System, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5468727		19951121	<--
APPLICATION INFO.:	US 1993-19359		19930216 (8)	<--
DISCLAIMER DATE:	20080218			
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1990-626579, filed on 13 Dec 1990, now patented, Pat. No. US 5187154, issued on 16 Feb 1993			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Warden, Jill			
ASSISTANT EXAMINER:	Salata, Carol A.			
LEGAL REPRESENTATIVE:	Arnold, White & Durkee			
NUMBER OF CLAIMS:	32			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	26 Drawing Figure(s); 25 Drawing Page(s)			
LINE COUNT:	1040			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a method of diagnosing and treating individuals
with diabetes or at risk to develop diabetes mellitus. In particular, gastric emptying determinations are used to assess risk. Risk or early symptoms associated with subsequent development of diabetes mellitus may
be controlled or alleviated by delaying gastric emptying. Delay or inhibition of gastric emptying is sufficient to restore gastric emptying
within normal ranges as determined by restoration of typical glucose metabolic parameters such as blood glucose and insulin levels to normal or near normal ranges. The method is also useful in prophylactic treatment of individuals at high risk to develop diabetes mellitus, such
as the obese, those with a family history of diabetes and those of particular ethnic and minority groups.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM4 . . . cholecystokinin (CCK) (Liddle, et al., 1988) and possible regulatory control by other gut hormones, such as VIP which stimulate insulin **release** from the pancreas (Schwartz, et al., 1990). It is known that CCK has a significant role in regulating glucose homeostasis.
. . . gastric emptying and reduces hyperglycemia (Jenkins, et al.,

L57 ANSWER 61 OF 79 USPATFULL on STN (Continued)
DETD . . . attenuates increases in postprandial plasma glucose in this model.
. . . intended scope of the invention. For example, other methods than drugs might be used to delay gastric emptying, such as **cellulose** derivatives and gastric bubbles. In addition, foods containing agents that delay gastric emptying such as trypsin inhibitors could be made.
.
.

L57 ANSWER 62 OF 79 USPATFULL on STN (Continued)
1990). However, the connection between CCK secretion on gastric emptying
and insulin **release** in normal and diabetic patients has not yet been fully evaluated (Liddle, 1990).
SUM8 Yet another aspect of the invention is a **pharmaceutical** composition which combines insulin and cholecystokinin in a vehicle suitable for injection or ingestion. This may be saline, a suitable.
SUM9 The invention also comprises a **pharmaceutical** composition of a compound that delays gastric emptying and an oral hypoglycemic in an orally acceptable **pharmaceutical** formulation. **Pharmaceutically** acceptable formulating agents include powders, granules, capsules, coated tablets, syrupy preparations and aqueous suspensions.
Formulating
agents employed may be solid. . . . but not limited to such solids as calcium phosphate, calcium carbonate, dextrose, sucrose, dextrin, sucrose ester, starch, sorbitol, mannitol, crystalline **cellulose**, talc, kaolin, synthetic aluminum silicate, carboxymethyl **cellulose**, **methylcellulose**, **ethyl cellulose** acetate phthalate, alginate, **polyvinyl** pyrrolidone, **polyvinyl** alcohol, gum arabic, tragacanth gum, gelatin, bentonite, agar powder, **shellac**, Tween 80, **carrageenans** and peyllium. Flavor enhancers may be added to oral preparations, including taste masking substances such as sweeteners and citrus flavors. . . .

DETD . . . Los Angeles, Calif. 90045). The assay for insulin was performed
by Smith Kline Bioscience Laboratory, St. Louis, Mo. by radioimmunoassay
(**Pharmacia** Diagnostics, Fairfield, N.J. 07004). Assays for GIP and CCK were performed by radioimmunoassay by the Gastroenterology Unit at Mayo Clinic. . . .
DETD . . . Acini were then incubated with plasma extracts (singlicates) or
standard CCK-8 concentrations (triplicates) for 30 min. at 37° C. Amylase **released** into the medium was assayed using potato yellow coupled starch as substrate. Amylase **released**, expressed as percentage of total amylase content, was compared to a dose-response curve for CCK-8 in order to calculate the.
DETD . . . parameters (i.e., glucose increment, gastric emptying, insulin and GIP) all changed in the direction suspected to occur with increased CCK **release**. The plasma CCK profile was surprising in that there was a very marked biphasic response to both test meals and.
DETD . . . mCi of .sup.99m Tc-SC. Each rat was tested with and without 1% cantocal, a trypsin inhibitor known to stimulate CCK **release**, in the glucose solution. Gastric emptying was monitored by gamma scintigraphy at 10 min intervals. Fasting and 1 hr postprandial. . .

DETD . . . to 65.1±5.7 min in lean nondiabetic rats. Results are illustrated in FIG. 21. Orally administered Camostat, a trypsin inhibitor (Ono **Pharmaceutical**s, Osaka, Japan) markedly slowed gastric emptying in both diabetic and lean rats, producing half-emptying times of 141±23 and 167±25 min. . . .
DETD . . . is human early Type 2 diabetes is reproduced in a rat model of non-insulin-dependent diabetes mellitus (NIDDM). Enhanced plasma CCK **release** by an oral trypsin inhibitor slows gastric emptying and

L57 ANSWER 62 OF 79 USPATFULL on STN
ACCESSION NUMBER: 95:84470 USPATFULL
TITLE: Films fabricated from mixtures of pectin and starch
INVENTOR(S): Fishman, Marshall L., Latrobe, PA, United States
Coffin, David R., Glenside, PA, United States
PATENT ASSIGNEE(S): The United States of America as represented by the Secretary of Agriculture, Washington, DC, United States
(U.S. government)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5451673		19950919	<--
APPLICATION INFO.:	US 1993-51415		19930423 (8)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Nutter, Nathan M.			
LEGAL REPRESENTATIVE:	Silverstein, M. Howard, Fado, John, Graeter, Janelle S.			
NUMBER OF CLAIMS:	17			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 9 Drawing Page(s)			
LINE COUNT:	539			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB High modulus, flexible films may be fabricated from blends of pectin, starch and, optionally, plasticizer. The films are biodegradable, water
soluble and are advantageous in that all materials are derived from agricultural products.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM4 . . . interest. These films are not only biodegradable but may also be recyclable as well as acceptable for human consumption and **pharmaceutical** applications. Multiple uses, ease of disposal and the replacement of petroleum-based raw materials with renewable agricultural
products make these types. . . .
SUM6 The film-forming properties of several water soluble polysaccharides have been studied. Films useful for **coatings** made from alginates and **carrageenans** were disclosed by Kester et al. (Food Technology, vol. 32(7), pp. 47-59, 1984). Paper coatings and sausage applications of carboxymethyl **cellulose** and other **cellulose** ethers have been investigated, and studies of chitin and chitosan films, including self-supporting films, have also been carried out (Averbach, . . . involved derivatized pectins used with divalent cations such as
calcium. A more recent work discussed blends of pectins and carboxymethyl **cellulose** for use as cigarette papers (Rind et al , U.S. Pat. No. 4,329,134 1978). U.S. Pat. No. 2,541,052 issued to M. . . .

SUM8 Starch has been investigated as a component in biodegradable films for applications such as agricultural mulch and **pharmaceutical** caplets (Otey et al., Ind. Eng. Chem. Prod. Res., Dev., vol. 16(4), pp. 305-308, 1977; Otey et al., Ind. Eng. . . .
DETD The novel films of the instant invention have a variety of applications.
They are useful as coatings, adhesives, controlled **release** carriers or

L57 ANSWER 62 OF 79 USPATFULL on STN (Continued)
food wrappings. Edible films are also contemplated and may be used for such purposes as the fabrication of bags containing soup mixes which are
added to boiling water for "instant" soup. A controlled **release** matrix which is water soluble also has numerous applications. In particular, **pharmaceutical** preparations may be applied to the skin. Biodegradable materials which are carrier matrices such as tablets or encapsulation materials are. . .

L57 ANSWER 63 OF 79 USPATFULL on STN
ACCESSION NUMBER: 93:84891 USPATFULL
TITLE: **Pharmaceutical** compositions containing orally absorbable glycosaminoglycans
INVENTOR(S): Cristofori, Manlio, Bologna, Italy
Marchi, Egidio, Casalecchio de Reno, Italy
Rotini, Leone C., Bologna, Italy
PATENT ASSIGNEE(S): Alfa Wassermann S.p.A., Alanno Scalo, Italy (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5252339		19931012	<--
APPLICATION INFO.:	US 1992-821455		19920115 (7)	<--
	NUMBER		DATE	
PRIORITY INFORMATION:	IT 1991-24		19910130	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Page, Thurman K.			
ASSISTANT EXAMINER:	Kishore, G. S.			
LEGAL REPRESENTATIVE:	Burkman and Archer			
NUMBER OF CLAIMS:	9			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	3 Drawing Figure(s); 3 Drawing Page(s)			
LINE COUNT:	587			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB **Pharmaceutical** compositions for oral use, preferably selected from capsules, tablets or sugar coated tablets, coated by an enterosoluble gastroresistant film, containing a lyophilizate consisting of therapeutically effective amounts of a glycosaminoglycan, a thickening substance and surfactants, and process for obtaining them. The compositions make possible the absorption of the orally administered glycosaminoglycans in the duodenum and in the intestine and the consequent performance of their anticoagulant, fibrinolytic, antithrombotic, antiatherosclerotic and antihyperlipoproteinemic properties.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI **Pharmaceutical** compositions containing orally absorbable glycosaminoglycans

AB **Pharmaceutical** compositions for oral use, preferably selected from capsules, tablets or sugar coated tablets, coated by an enterosoluble gastroresistant film, containing.

SUM4 For quite a time many remarkable efforts are carried out in order to fine adjuvant substances or derivatives or **pharmaceutical** formulations suitable for increasing their oral bioavailability, due to the great therapeutic interest that the glycosaminoglycans have in the prevention.

SUM4 . . . [Jarret et al., Thromb. Diath. Haemorrh., 25, 187-200, (1971)]

L57 ANSWER 63 OF 79 USPATFULL on STN (Continued)
or nitric acid [Soe T. K. et al, Can. J. Physiol. **Pharmacol**., 54, (6) 613-7, (1976)].

SUM4 . . . solutions of heparin, a vegetable oil and ionic or non ionic surfactants into the duodenum of the experimental animals [J. **Pharm**. Sci., 59, 706-10 and 1372-5, (1969)].

SUM4 More recently, they tried to help the absorption by using suitable **pharmaceutical** formulations based on liposomes as vehicles for the glycosaminoglycans [Masaharu Ueno et al., Chem. **Pharm**. Bull., 30, (6), 2245-7, (1982), Belgian patent BE 860,011, French patent FR 2,492,259] or by doing some complexes with quaternary.

SUM4 Notwithstanding all these attempts, the need of finding new kinds of oral **pharmaceutical** formulations containing glycosaminoglycans endowed with better bioavailability, still exists.

SUM4 The present invention constitutes a valid answer to this problem; in fact it was discovered that orally administrable **pharmaceutical** compositions, for instance tablets, capsules or sugar coated tablets, coated with an enterosoluble gastroresistant film, containing a lyophilizate made by.

SUM4 **Pharmaceutical** compositions for oral use coated with an enterosoluble gastroresistant film, containing a lyophilizate made by therapeutically effective amounts of a.

SUM4 **Pharmaceutical** compositions for oral use preferred in the fulfilment of the present invention are tablets, capsules and sugar coated tablets.

SUM4 The process for obtaining said **pharmaceutical** compositions and their therapeutic use in the prevention and treatment of the thrombotic and atherosclerotic pathologies are also object of.

SUM4 a) enterosoluble gastroresistant coating of the **pharmaceutical** compositions that enables the active principle to unaltered cross the gastric juices, in which the glycosaminoglycans are not very much. .

SUM4 The obtained experimental data clearly show the oral absorption in man of the **pharmaceutical** compositions described in the invention and therefore they allow the use of these compositions in the prevention and
treatment of. . .

SUM4 . . . principle, together with a thickening substance and surfactants.
as adjuvants of the absorption is the first step in preparing the **pharmaceutical** forms for the object of the present invention. The thickening agent is dissolved under heating and stirring in distilled. . .

SUM4 . . . of the silicic anhydrides. Gum arabic, tragacanth, xanthan gum,
pectins, starchs, carrageenans, alginates, gelatin and oasein from the natural polymers, **hydroxyethylcellulose**, **methylcellulose**, **hydroxypropylcellulose** and **carboxymethylcellulose** from the modified natural polymers, **polyvinylpyrrolidone** and **polyvynilic** alcohol from the vinyl polymers, Carbopol® from the carboxyvinyl polymers, hydrogenated castor oil named Cutina® HR from the esters of. . .

SUM4 The preparation of the enterosoluble gastroresistant **pharmaceutical** compositions for oral use containing the above described lyophilizate is
the second step of the process.

SUM4 The different **pharmaceutical** forms for oral use not coated by the protective film are prepared according to known methods. For instance the tablets. . . surfactants, mixed with excipients like maize starch

L57 ANSWER 63 OF 79 USPATFULL on STN (Continued)
and lactose. The so obtained granulate is mixed with other excipients like microcrystalline **cellulose**, reticulated **polyvinylpyrrolidone** and magnesium stearate and then is compressed in order to obtain a normal tablet.

SUM4 . . . or capsules obtained with known methods, are submitted to the gastroprotective treatment. In case the sugar coated tablets are the **pharmaceutical** form, the tablets are submitted to sugar coating according to known methods, after the gastroprotective treatment.

SUM4 . . . first, non-protective, coating, that serves as support to obtain an optimal distribution of the protective gastroresistant enterosoluble film on the **pharmaceutical** form, is carried out before putting into effect the coating by means of the gastroresistant enterosoluble film.

SUM4 This non-protective coating is carried out by spraying on the **pharmaceutical** forms in coating pan a suspension made by **hydroxypropylmethylcellulose**, polyethylene glycol 6000, titanium dioxide and talc in a 22:1 mixture of 95% ethyl alcohol and water, in such an.

SUM4 . . . be used to obtain a gastroresistant enterosoluble coating. The coating substances preferred in the fulfillment of the present invention
are **cellulose** acetate, the copolymers of the methacrylic acid and of the methacrylic esters in different ratios, commercially known under the
trademark Eudragit®, **polyvinylacetophthalate** and **hydroxypropylmethylcellulose** phthalate.

SUM4 . . . more plasticizers in a 80:1 mixture of ethyl alcohol and water and spraying this solution in coating pan on the **pharmaceutical** forms previously coated with the non-protective coating, in such an amount that the weight of the gastroresistant enterosoluble film is comprised between 24 and 30% as to the weight of the non-coated **pharmaceutical** form.

SUM4 The so obtained gastroresistant enterosoluble **pharmaceutical** forms make possible the absorption of the glycosaminoglycans they contain as it is clearly shown by some tests on the.

DETD . . . FIGS. 1, 2 and 3, clearly show the absorption of the orally administered sulodexide by means of one of the **pharmaceutical** formulations object of the invention. In fact the experimental data already show the fibrinolytic effect of the sulodexide one hour. . .

DETD TABLE 1

Fibrinolytic activity in man of 200 mg of sulodexide orally administered by means of the **pharmaceutical** formulation described in Example 5 (n X s.e.)

TIME (hours)	FIBRIN PLATES ANTIGEN (mm diam. lyzis)	PAI FUNCTIONAL (ng/ml)	(AU/ml)
0	32.9 X. . .		
DETD . . . of each tablet			

Glucuronylglycosaminoglycan sulfate . . . 100 mg
Saccharose monoplmitate 50 mg
Sodium lauryl sarcosinate 50 mg

L57 ANSWER 63 OF 79 USPATFULL on STN (Continued)

Xanthan gum	20 mg
Maize starch	93.8 mg
Lactose	91.5 mg
Microgranular **cellulose**	300 mg
Reticulated **polyvinylpyrrolidone**	
	100 mg
Magnesium stearate	10 mg
Hydroxypropylmethylcellulose	
	14 mg
Polyethylene glycol 6000	0.8 mg
Titanium dioxide	3.2 mg
Talc	3.0 mg
Hydroxypropylmethylcellulose phthalate	
	36 mg
Acetylated monoglycerides	
	3.2 mg

DETD . . . and sifted on a sieve having meshes equal to 0.8 mm. The so obtained granulate is mixed together with microgranular **cellulose**, reticular **polyvinylpyrrolidone** and magnesium stearate and the resulting mixture is tabletted. The tablets are coated in coating pan by

means of a . . . alcohol and water. Subsequently the gastroresistant enterosoluble coating is carried out by spraying in the coating pan a solution of **hydroxypropylmethylcellulose** phthalate and acetylated monoglycerides in a 80:1 mixture of ethyl alcohol and water on the tablets coated with the first. . .

DETD

Composition of each capsule

Glucuroxylglycosaminoglycan sulfate	
	100 mg
[sulodexide]	
Saccharose monopalmitate	50 mg
Sodium laurylsarcosinate	50 mg
Xanthan gum	20 mg
Caprilo-capric glycerides	
	380 mg
Hydroxypropylmethylcellulose	
	15 mg
Polyethylene glycol 6000	0.6 mg
Titanium dioxide	2.4 mg
Talc	2.4 mg
Hydroxypropylmethylcellulose phthalate	
	24 mg
Acetylated monoglycerides	
	2.4 mg

DETD . . . soft gelatin type 10 oval capsules. These capsules are first coated in coating pan with a first film made by **hydroxypropylmethylcellulose**, polyethylene glycol 6000, titanium dioxide and talc suspended in a 22:1 mixture of 95% ethyl alcohol and water. The gastroresistant enterosoluble coating is subsequently carried

L57 ANSWER 63 OF 79 USPATFULL on STN (Continued)

Acetylated monoglycerides	
	1.6 mg
Gum arabic	7 mg
Saccharose	138 mg
Carnauba wax	0.2 mg
White wax	0.1 mg

DETD . . . is dry granulated and sifted on a sieve having meshes of 0.8 mm. The obtained granulate is mixed with microgranular **cellulose**, reticulated **polyvinylpyrrolidone** and magnesium stearate and the mixture is tabletted. The obtained tablets are coated in coating pan with a first film made by a mixture containing 7 g of **hydroxypropylmethylcellulose**, 0.4 g of polyethylene glycol 6000, 1.6 g of titanium dioxide and 1.6 g of talc suspended in a 22:1. alcohol and water. Subsequently the gastroresistant enterosoluble coating is carried out by spraying in the coating pan a solution of **hydroxypropylmethylcellulose** phthalate and acetylated monoglycerides in a 80:1 mixture of ethyl alcohol and water on the tablets coated by the first. .

DETD . . . of each tablet

Sodium heparin	100 mg
Saccharose monopalmitate	50 mg
Sodium laurylsarcosinate	50 mg
Xanthan gum	20 mg
Maize starch	93.8 mg
Lactose	81.5 mg
Microgranular **cellulose**	300 mg
Reticulated **polyvinylpyrrolidone**	
	100 mg
Magnesium stearate	10 mg
Hydroxypropylmethylcellulose	
	14 mg
Polyethylene glycol 6000	0.8 mg
Titanium dioxide	3.2 mg
Talc	3.0 mg
Hydroxypropylmethylcellulose phthalate	
	32 mg
Acetylated monoglycerides	
	3.2 mg

CLM What is claimed is:

1. A **pharmaceutical** composition for oral use in unit dosage form which consists of a) a coating, b) a non-coated portion, and c) . . . interposed between said lyophilizate and said gastroresistant enterosoluble film and being obtained by spraying a suspension of

3-5-21

mgs of **hydroxypropylmethylcellulose**, 0.2-1.2 mgs of polyethylene glycol 6000, 0.8-4.8 mgs of titanium dioxide and 0.8-4.8 mgs of talc in a 22:1 mixture.

CLM What is claimed is:

2. The **pharmaceutical** composition according to claim 1 wherein said non-coated portion b) comprises a lyophilizate, said lyophilizate consisting of 200 mgs of . . . monopalmitate, and 50 mgs of sodium lauryl sarcosinate, said coating a) being a gastroresistant enterosoluble film consisting of 24 mgs **hydroxypropylmethylcellulose** phthalate and 2.4 mgs of acetylated monoglycerides, said non-protective coating c) consisting of 10.5 mgs of **hydroxypropylmethylcellulose**, 0.4

L57 ANSWER 63 OF 79 USPATFULL on STN (Continued)

out by spraying in the coating pan a solution of **hydroxypropylmethylcellulose** phthalate and acetylated monoglycerides in a 80:1 mixture of ethyl alcohol and water on the capsules coated with

the first. . .

DETD

Composition of each capsule

Low molecular weight dermatan sulfate	
	200 mg
Saccharose monopalmitate	100 mg
Sodium laurylsarcosinate	50 mg
Sodium glycinate	20 mg
Hydroxypropylmethylcellulose	
	10.5 mg
Polyethylene glycol 6000	0.6 mg
Titanium dioxide	2.4 mg
Talc	2.4 mg
Hydroxypropylmethylcellulose phthalate	
	24 mg
Acetylated monoglycerides	
	2.4 mg

DETD . . . 31% (w/v) aqueous gelatin solution and then are coated in coating pan by means of a first film made by **hydroxypropylmethylcellulose**, polyethylene glycol 6000, titanium dioxide and talc suspended in a 22:1 mixture of 95% ethyl alcohol and water. Subsequently the gastroresistant enterosoluble coating is carried

out by spraying in the coating pan a solution of **hydroxypropylmethylcellulose** phthalate and acetylated monoglycerides in a 80:1 mixture of ethyl alcohol and water on the capsules coated with

the first.

DETD . . . tablet

Low molecular weight heparin	
	50 mg
Saccharose monopalmitate	25 mg
Sodium laurylsarcosinate	25 mg
Xanthan gum	10 mg
Maize starch	17 mg
Lactose	41 mg
Microgranular **cellulose**	150 mg
Reticulated **polyvinylpyrrolidone**	
	50 mg
Magnesium stearate	5 mg
Hydroxypropylmethylcellulose	
	7 mg
Polyethylene glycol 6000	0.4 mg
Titanium dioxide	6.4 mg
Talc	5.8 mg
Hydroxypropylmethylcellulose phthalate	
	16 mg

L57 ANSWER 63 OF 79 USPATFULL on STN (Continued)

mgs polyethylene glycol 6000, 2.4 mgs. of titanium dioxide and 2.4 mgs. of talc.

CLM What is claimed is:

. . . the group consisting of copolymers of the methacrylic acid and of the

methacrylic esters in different ratios known as Eudragit®, **polyvinylacetophthalates** and **hydroxypropylmethylcellulose** phthalate and at least one plasticizer which is a member selected from the group consisting of diethylphthalate, triacetin, polyethylene glycols. . . .

CLM What is claimed is:

. one member selected from the group consisting of gum arabic, gum tragacanth, xanthan gum, pectins, starch, carrageenans, alginates, casein, gelatin, **hydroxycellulose**, **methylcellulose**, **hydroxypropylcellulose**, **carboxymethylcellulose**, **polyvinylpyrrolidone**, polyvinyl alcohol, carbomyvinyl polymers known as Carbopol®, hydrogenated castor oil and aluminum oxide monostearate.

CLM What is claimed is:

9. A **pharmaceutical** composition for oral use in unit dosage form which consists of a) a coating, b) a non-coated portion, c) a. . . . interposed between said lyophilizate and said gastroresistant enterosoluble film and being obtained by spraying a suspension of

3.5-21

mgs of **hydroxypropylmethylcellulose**, 0.2-1.2 mgs of polyethylene glycol 6000, 0.8-4.8 mgs of titanium dioxide and 0.8-4.8 mgs of talc in a 22:1 mixture.

IT Glycosaminoglycans, uses

(enteric-coated **pharmaceutical** composition containing)

IT Surfactants

IT Thickening agents

(enteric-coated **pharmaceutical** composition of glycosaminoglycans containing)

IT Acrylic polymers

IT Bile salts

IT Carboxylic acids, uses

IT Caseins, uses

IT Gelatin, uses

IT Phospholipids, uses

IT Polyoxyalkylenes

(enteric-coated **pharmaceutical** composition of glycosaminoglycans containing)

IT **Pharmaceutical** dosage forms

(capsules, enteric-coated, of glycosaminoglycans and thickeners and surfactants)

IT Oligosaccharides

(di-, esters, with fatty acids, enteric-coated **pharmaceutical** composition of glycosaminoglycans containing)

IT Monosaccharides

(esters, with fatty acids, enteric-coated **pharmaceutical** composition of glycosaminoglycans containing)

IT Fatty acids, esters

(esters, with saccharides and ethoxylated alcs., enteric-coated **pharmaceutical** composition of glycosaminoglycans containing)

IT Alcohols, compounds

(ethoxylated, with fatty acids, enteric-coated **pharmaceutical**

L57 ANSWER 63 OF 79 USPATFULL on STN (Continued)
compd. of glycosaminoglycans contg.)
IT Castor oil
(hydrogenated, enteric-coated **pharmaceutical** composition of glycosaminoglycans containing)
IT Glycerides, compounds
(mono-, acetates, enteric-coated **pharmaceutical** composition of glycosaminoglycans containing)
IT **Pharmaceutical** dosage forms
(tablets, enteric-coated, of glycosaminoglycans and thickeners and surfactants)
IT 9005-49-6, Heparin, uses 9005-49-6D, Heparin, alkali and alkaline-earth
salts 9041-08-1, Sodium heparin 24967-94-0, Dermatan sulfate 37821-29-1, Sclerodermin
(enteric-coated **pharmaceutical** composition containing)
IT 64-86-8, Diethylphthalate 77-74-1, Triacetin 145-42-6, Sodium taurocholate 361-29-1, Sodium cholate 863-57-0, Sodium glycocholate 7431-95-3, Sodium lauryldecanoate 7644-93-90, Sulfuric acid, derivs. 9000-91-5, Gum arabic **9000-07-1**, Carrageenan 9000-65-1, Gum tragacanth 9000-69-5, Pectin 9002-89-5, Poly(vinyl alcohol) 9003-39-8, Pvp 9004-32-4, Carboxymethyl **cellulose** 9004-35-7, **Cellulose** acetate 9004-62-0, Hydroxyethyl **cellulose** 9004-64-2, Hydroxypropyl **cellulose** 9004-65-3, Methyl **cellulose** 9005-25-8, Starch, uses 9005-32-7D, Alginic acid, derivs. 9005-63-6D, derivs. 9007-20-9, Carbopol 11138-66-2, Xanthan gum 13419-15-9 25322-68-3, Polyethylene glycol 26446-38-8, Saccharose monopalmitate 53237-50-6
(enteric-coated **pharmaceutical** composition of glycosaminoglycans containing)
IT **9000-07-1**, Carrageenan
(enteric-coated **pharmaceutical** composition of glycosaminoglycans containing)

L57 ANSWER 64 OF 79 USPATFULL on STN (Continued)
SUMM The invention also comprises a **pharmaceutical** composition of a compound that delays gastric emptying and an oral hypoglycemic in an orally acceptable **pharmaceutical** formulation. **Pharmaceutically** acceptable formulating agents include powders, granules, capsules, coated tablets, syrupy preparations and aqueous suspensions. Formulating
agents employed may be solid. . . but not limited to such solids as calcium phosphate, calcium carbonate, dextrose, sucrose, dextrin, sucrose ester, starch, sorbitol, mannitol, crystalline **cellulose**, talc, kaolin, synthetic aluminum silicate, carboxymethyl **cellulose**, **methylcellulose**, cetostearyl alcohol, alginates, **polyvinyl** pyrrolidone, **polyvinyl** alcohol, gum arabic, tragacanth gum, gelatin, bentonite, agar powder, **shellac**, Tween 80, **carrageenans** and pyrillian. Flavor enhancers may be added to oral preparations, including sweeteners such as saccharin and citrus flavors. . .
DETD Sources of drugs and materials are as indicated. Bowman-Birk trypsin inhibitor is available from Nestech, Ltd. Devey, Switzerland. CNA **Pharmaceuticals**, Ltd., Washa, Sayre, may be contacted for availability of another trypsin inhibitor, Camostate.
DETD . . . Los Angeles, CA 90045). The assay for insulin was performed by Smith Kline Biosciences Laboratory, St. Louis, MO by radioimmunoassay (**Pharmacia** Diagnostics, Fairfield, NJ 07004). Assays for GIP and CCK were performed by radioimmunoassay by the Gastroenterology Unit at Mayo Clinic.
DETD . . . intended scope of the invention. For example, other methods than drugs might be used to delay gastric emptying, such as **cellulose** derivatives and gastric bubbles. All such modifications are intended to be within the scope of the claims.
CLM What is claimed is:
4. The method of claim 1 wherein the therapeutically effective dose of cholecystokinin comprises an injectable **pharmaceutical** carrier.

L57 ANSWER 64 OF 79 USPATFULL on STN
ACCESSION NUMBER: 93:12512 USPATFULL
TITLE: Diagnosis and treatment of humans with diabetes or at risk to develop diabetes
INVENTOR(S): Phillips, William, San Antonio, TX, United States
Schwartz, Joyce G., San Antonio, TX, United States
PATENT ASSIGNEE(S): Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5187154		19930216	<--
APPLICATION INFO.:	US 1990-626579		19901213 (7)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Cashion, Jr., Merrell C.			
ASSISTANT EXAMINER:	Celsa, E.			
LEGAL REPRESENTATIVE:	Arnold, White & Durkee			
NUMBER OF CLAIMS:	4			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	10 Drawing Figure(s); 10 Drawing Page(s)			
LINE COUNT:	589			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a method of diagnosing and treating individuals
with diabetes or at risk to develop diabetes mellitus. In particular, gastric emptying determinations are used to assess risk. Risk or early symptoms associated with subsequent development of diabetes mellitus may
be controlled or alleviated by delaying gastric emptying. Delay or
The Government may have certain rights in the invention pursuant to grant Number: 2-507-RR07187-11.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . diabetes mellitus by first determining gastric emptying patterns and then treating with an appropriate drug. Treatment comprises
administration of a **pharmaceutical** preparation having the ability to inhibit or block gastric emptying. In particular, drugs that affect gut motility are useful as . . .
SUMM . . . the role of cholecystokinin (CCK) (12) and possible regulatory control by other gut hormones, such as VIP which stimulate insulin **release** from the pancreas (9). It is known that CCK has a significant role in regulating glucose homeostasis in humans (13). . . . that it delays gastric emptying and reduces hyperglycemia (14). However, the connection between CCK secretion on gastric emptying and insulin **release** in normal and diabetic patients has not yet been fully evaluated (10).
SUMM Yet another aspect of the invention is a **pharmaceutical** composition which combines insulin and cholecystokinin in a vehicle suitable for injection This may be saline, a suitable buffer such. . .

L57 ANSWER 65 OF 79 USPATFULL on STN
ACCESSION NUMBER: 92:92526 USPATFULL
TITLE: Controlled **release** interpronmal delivery system
INVENTOR(S): Hill, Jay Clay CT., Locust, NJ, United States 07760
White, Robert D., 65 Glen Gray Rd., Oakland, NJ, United States 07436

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5165913		19921124	<--
APPLICATION INFO.:	US 1991-762353		19910829 (7)	<--
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1989-453302, filed on 20 Dec 1989, now abandoned And a continuation-in-part of Ser. No. US 1988-270132, filed on 14 Nov 1988, now abandoned And a continuation-in-part of Ser. No. US 1988-270135, filed on 14 Nov 1988, now abandoned And a continuation-in-part of Ser. No. US 1988-270167, filed on 14 Nov 1988, now abandoned And a continuation-in-part of Ser. No. US 1988-270167, filed on 14 Nov 1988, now abandoned And a continuation-in-part of Ser. No. US 1988-270544, filed on 14 Nov 1988, now abandoned And a continuation-in-part of Ser. No. US 1988-270722, filed on 14 Nov 1988, now abandoned And a continuation-in-part of Ser. No. US 1988-270562, filed on 14 Nov 1988, now patented, Pat. No. US 4911927
DOCUMENT TYPE:	UTILITY			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Page, Thurman K.			
ASSISTANT EXAMINER:	Harrison, Robert H.			
LEGAL REPRESENTATIVE:	Linek, Ernest V.			
NUMBER OF CLAIMS:	9			
EXEMPLARY CLAIM:	1			
LINE COUNT:	1886			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention discloses dental floss containing surfactant and silicone preparations with added chemotherapeutic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Controlled **release** interpronmal delivery system

SUMM . . . containing chemotherapeutic agents, e.g., antimicrobials, antibiotics, anticoulants, desensitizers, and anti-tartar agents, such as tetracycline, chlorhexidine, sodium fluoride, stannous fluoride, and **polyvinyl** pyrollidone iodine complex with iodine.
SUMM The present invention is based upon the discovery that this type of mechanical action can be supplemented by the **release** of surfactants from the floss into the interpronmal region. These **released** surfactants are readily solubilized in saliva and interpronmal fluids to produce a detersive effect in the interpronmal region during flossing. . . .
SUMM (3) Ser. No. 07/270,164 --Filed Nov. 14, 1988, entitled Method of Treating the Oral Cavity with Dental Floss Containing **Polyvinyl** Pyrollidone Iodine Complex, now abandoned;
SUMM . . . and follow the contours of the teeth during flossing/cleaning. This improved mechanical cleaning is further supplemented with various insoluble abrasives **released** interpronmally from the floss during

L57 ANSWER 65 OF 79 USPATFULL on STN (Continued)
flossing. This combination of abrasive, surfactant and mechanical action
is more efficient than mechanical action.
SUM94 . . . the floss is positioned between teeth, the pressure applied during flossing. When the floss is splayed, the loaded substances are **released** and continue to be **released** during the sawing motion of flossing. This **releasing** action supplements the cleaning action of flossing by **releasing** cleaners to work with the floss.
SUM96 iii. said interproximal delivery system **release** from between about 10 and about 90% by weight of said cleaning agents produced upon agingin; and
SUM98 The following features of the present invention characterize the surfactant/silicone/abrasive mixture that is produced when flossing interproximally: 1. Rapid **release** of substantial quantities of saliva soluble surfactant, silicone and abrasive when the floss is pulled across tooth surfaces. The construction . . . of unbonded floss, the absence of wax and a unique surface which exposes the fibers to open up and **release** the load during flossing.
SUM99 With the advent of "tooth friendly" tartar control into floss for **release** during flossing as discussed below, the opportunity is available to include desensitizing agents into the load to minimize flossing pain.
. . . desensitizing agents such as strontium chloride are used in dentifrices for "sensitive" teeth. These substances produce a comparable
effect when **released** interproximally from the floss of the present invention. This desensitizing effect further improves the overall hedonics of the floss of.
SUM99 This spreading out during flossing, also triggers the **release** mechanism which discharges most of the load interproximally during flossing, i.e., up to about 90% by weight. The . . . surfactant/silicone/abrasive mixture thus, **released** is readily solubilized in the saliva and other fluids present. This solubilized mixture responds to the separate mechanical action of. . . to take up
SUM99 **Release** of the load leaves spaces in the floss which tend . . . to take up and hold some of the microscopic substances.
SUM99 Up to about 90% of this load is **released** onto interproximal and subgingival sites during flossing, i.e., up to about 64 mg/yd. This **release** of surfactant into the sites cleans the tooth surfaces and saturates with flosses sold today. The flosses of the present invention. . .
SUM99 Additionally, the floss of the present invention can contain therapeutic
substances for **release** at concentrations up to 40 mg/yd. When these substances are included in the load they are **released** onto those interproximal and subgingival sites which cannot be reached by rinsing or brushing. This interproximal **release** of substances in these concentrations is unique, in that it improves plaque control and gingivitis scores over other dental flosses.
SUM99 a. chemical cleansing with surfactants **released** form the floss of the present invention,
SUM99 b. prolonged modification of the surface chemistry of the microfibrs by the coating materials **released**, e.g., silicones, **released** from the floss, and
SUM99 c. alteration of microflors with various active ingredients contained in

L57 ANSWER 65 OF 79 USPATFULL on STN (Continued)
the load and **released** during flossing.
SUM99 b. abrasive, disruption with abrasives **released** from floss including: silica, dicalcium phosphate, pyrophosphates etc., at concentrations up to 60 mg/yd; and
SUM99 c. surfactant disruption resulting from the **release** of surfactants during flossing.
SUM99 a. chemical cleansing with surfactants **released** from the floss,
SUM99 c. alteration of the plaque with various active ingredients contained in
the load and **released** during flossing including: tetrasodium pyrophosphate, tetrapotassium pyrophosphate etc.
SUM99 b. abrasive removal by the abrasives **released** from the floss including: silica, dicalcium phosphate, pyrophosphates etc., and
SUM99 b. cleansing resulting from the **release** of surfactants during flossing.
SUM99 (for "starchier"). Most dental tests implicate plaque in the formulation of caries, or tooth decay. In addition, these embedded bacteria **release** toxins that cause gingivitis, bleeding and swelling of the gum. Gingivitis can lead to periodontitis in which gums recede, pockets.
SUM99 . . . and tartar control and have little access to the critical interproximal area. In contrast, the floss of the present invention **releases** substances interproximally and **subgingivally**. Additionally, some of these preparations such as mouth rinses and prerinses contain various antimicrobial substances which.
SUM99 . . . concentrations; considering that the compositions of the present invention are not soluble in the floss. Secondly, floss so treated will "**release**" these compositions during flossing and chemically cleanse the area of plaque and bacterial precursors, bacteria, etc., while coating teeth and gum surfaces with a plaque matrix disrupting substance. The **release** of these substances is particularly effective in disrupting, for prolonged periods, the plaque matrix on those interproximal sites. The cleansing effect results from the compositions **released** from the floss also takes place on those interproximal surfaces the brushing does not reach. This chemical cleansing and matrix disruption.
DETD 8. retain various flavors, sweeteners and **pharmacologically** preparations active on surfaces of the mouth imparting an unexpected prolonged effect of the **pharmacologically** active ingredient as well as prolonged flavor perception, and
DETD Furthermore, the cleaner, coating substance, and saliva or gingival crevice fluid mixture obtained when the compositions are **released** in the mouth are ingestible and can be pleasantly swallowed, which further distinguishes it from typical oral cleaning compositions used. . . . the mouth with foam and can be pleasantly swallowed which is necessary for those flosses loaded with substantial quantities of **releasable** materials.
DETD The compositions **released** from the floss during flossing can disrupt plaque formation without resort to antimicrobial ingredients. The various surfaces of teeth and gums are coated with a smooth thin film **released** from the floss which prevents plaque formation. These coatings remain in the interdental spaces for extended periods and prolong this.
DETD Thus, the floss may additionally comprise one or more chemotherapeutic agents, for example, tetracycline, chlorhexidine,

L57 ANSWER 65 OF 79 USPATFULL on STN (Continued)
sodium fluoride, stannous fluoride, and/or **polyvinyl** pyrrolidine iodine complex, to mention but a few. Given the teachings of this disclosure, the skilled artisan will readily be
DETD The floss of the present invention is unique in its capacity to **release** the "loaded" compositions interproximally. Unexpectedly, the property of **releasing** these compositions correlates directly with the spacing up and/or fluffing of the treated floss strands during flossing. This tendency of the
DETD . . . delicate gum tissue. Furthermore, the loaded floss of the present invention, opens up tends to conform to surfaces and **releases** the loaded substances during flossing. The loaded floss of this **release** mechanism results in:
DETD 3. the floss strands continuing to **release** the loaded substances during flossing as the floss is moved over teeth, under the gum line and
over the interproximal.
DETD Thus, the **release** mechanism of the floss of the present invention allows the floss to reach the interproximal sites and physically remove plaque, while at the same time depositing the composition of the present invention interproximally to assist in cleaning and/or treating these interproximal sites. This **releasing** of the compositions was quantified as follows:
DETD . . . of floss was again dried at 104° F. for two hours and reweighed. The average quantity of loaded active ingredients **released** was established at 18 mg/yd with no significant variation between individuals or between pieces of floss.
DETD . . . containing water-insoluble antimicrobial substances offers the opportunity to disrupt subgingival microflora and limit regrowth while also controlling supragingival plaque. The **release** interproximally and subgingivally of substantive chemotherapeutic antimicrobials and the plaque disrupting composition from the present invention from the floss of.
DETD Surprisingly, the cleaning/coating compositions **released** from the floss of the present invention retain good surface active properties and
are able to clear the interproximal areas.
DETD 2. The treated floss **releases** the compositions of the present invention onto surfaces of teeth and gums more effectively cleaning the interproximal sites.
DETD 7. The **released** compositions condition teeth and gums and leave the mouth feeling exceptionally clean and smooth. The surfaces of the teeth are . . . polo[heart flavor] compositions are generally described as "freshness" and is stronger, more natural tasting and persists tooth longer with the **released** compositions of the present invention than when state-of-the-art, encapsulated "flavored" flosses are used under comparable conditions.
DETD . . . longer-than-expected time period thus enhancing the "it's working" perception without negative "dirty mouth" connotations due to the bad taste of **released** plaque and debris. The latter is found to reduce frequency of use and undermine the regular cleansing advantage.
DETD . . . to be beneficial towards plaque control and are included in the
compositions of this invention. See, for example, Segal, J. **Pharm.** Sci., 74: 79-81 (1985) and Waldbaum, J. Am. Dent. Assoc., 111: 740-741 (1985)
DETD . . . and not commonly used in floss, can be selected from natural and synthetic gums such as: carrageenan, gum tragacanth, methyl **cellulose** and derivatives there of such as hydroxyethyl methyl

L57 ANSWER 65 OF 79 USPATFULL on STN (Continued)
cellulose, **polyvinyl** pyrrolidone, and hydrophilic carboxyvinyl polymers such as those sold under the trademark Carbopol 934.
DETD . . . or wax floss do not provide for the quantity of load required for the present invention nor the "controlled **release**" of this loaded material interproximally for prolonged periods. The pressures used for waxing, for example, primarily coat the outer surfaces of. .
DETD . . . to from between about 10 mg and about 100 mg per yard of floss.
These loaded substances are then controllably **released** into the oral cavity during flossing at the preferred load of about 18 mg/yd of the load. For example, a floss containing 40 mg/yd of load will **release** between about 20 and about 32 mg of load during flossing. Note, the
rate of **release** of these loaded active ingredients is easily controlled by varying the floss construction, the process of loading, and the composition
DETD . . . careful examination, primarily "coating". Thus, the pressures and forces encountered during flossing allow for the loaded material to be progressively **released** interproximally between the teeth and under the gum line. This "interstitial loading" is particularly critical in order to avoid "stripping".
DETD . . . worked through the contact point and moved gently under the gumline the loaded substances of the present invention are continually **released** into those areas where plaque and debris are difficult to clean and where irritation bleeding and bacterial infection tend to.
DETD . . . all these Examples the surfactant used was Fluvonic F 127, the coating composition Dow Corning Silicone 1491, the Flavor FPI 101. **Carrageenan** was included in the loading composition in all examples. The results are set out in Table III below.

EXAMPLE	FLAVOR (ml)					OTHER	GLYCERINE/	
	SILICONE SACCHARIN		SORBITOL	ADDITIVES				
	in g.	in g.	in g.	in g		FLOSS TYPE	RESULTS	
5	10.8/7.2	0/1.	3.5/2	**Carrageenan** 0.5		Unwaxed nylon	Dusting dramatically improves mouth feel	
6	15.8/7.2	0/1.	8/2	**Carrageenan** 5		Unwaxed nylon	Improves mouth feel	
7	29.7/16.8		0/2.66	19.6/4.7	**Carrageenan** 1.77	Unwaxed nylon powder	Note in loading there are a simple peas thru the chamber. Load was 250 mg/25 yd dry to touch.	
8	29.7/16.8		--/2.66	19.6/4.7	**Carrageenan** 1.77			

L57 ANSWER 65 OF 79 USPATFULL on STN (Continued)
Oriented poly-
Load was 2000 mg/25 yd
pre gelled plus
eater 150/68/4
Dry to touch.
powder to dry

DETD TABLE V

EX- CLEANER **COATING** SORBITOL
CARRAGEENAN
BICALCIUM PHOSPHATE
AMPLE (%) COMPOSITION (%)
(%) VISCOSIFIER (%)
DENTAL ABRASIVE
FLAVOR

4G P&G Stearite/
Silicone glycol/ZO
10 10 15 5
4G
41. . .
DETD In contrast, when the **polyvinyl** pyrolildone iodine complex is included in the preparations loaded into the floss of the present invention, the effect on . . . .
DETD The **polyvinyl** pyrolildone iodine complex is a stable, effective antimicrobial with minimal staining that is ideally suited for addition to the floss. . .
DETD 2. The required amount of **polyvinyl** pyrrolidone-iodine complex is added with vigorous mixing to achieve full dispersion, then immediately.
DETD TABLE VII

Surfactant
Coating Iodine,
Fluorenc
Substance Flavor Anticolacnsns
Iodine salt, or
F127 Silicone
Sorbitol
Saccharin
IFF **101**
Carrageenan
Silica
Propyl Gallate
Iodine Complex
in % 150G xn %
xn % in % in % in % in %
in.
DETD . . . about 60 wg/yd to about 30 ng/yd, the pathogenic microflora of infected sires can generally be controlled. Generally, the tetragoline **released** for each interproximal surface floased is between about 3 mg and about 30 mg, with total **release** for all 60 surfaces requiring at least about 64 mg/yd.

L57 ANSWER 65 OF 79 USPATFULL on STN (Continued)
(percent by weight)
Surfactant
Coating
Sorbitol Flavor SnF.sub.2
Fluronic
Substance
Polyol/SnF.sub.2
Acid IFF Antioxidants
Concentration
F127 Silicone
Solution
Saccharin
101 Carrageenan
Silica
Propyl Gallate
in melt-emulsion
in % 1500 xn %
in % in % xn %
in.
DETD . . . . is expected that the long dodecene chain could be expected to influence substantivity and retention in the oral cavity. Controlled **release** of the free base chlorhexidine is expected which in turn is substantive to the teeth and guns /a primary requirement. . . .
DETD TABLE XI

Surfactant
Coating Flavor Chlorhexidine
Fluronic
Substance IFF Concentration
F127 Silicone
Chlorhexidine
Saccharin
101 Carrageenan
Silica
Sorbitol
in melt-emulsion
in % 1500 xn %
compound (2)
in % in %
in % in % in %. . .
DETD TABLE XII

Surfactant
Coating
Sorbitol Flavor NaF.sub.2
Fluronic
Substance
NaF.sub.2 IFF Antioxidants
Concentration
F127 Silicone
Solution
Saccharin
101 Carrageenan
Silica
Propyl Gallate
in melt-emulsion
in % 1500 xn %

L57 ANSWER 65 OF 79 USPATFULL on STN (Continued)
DETD

Surfactant
Coating
Fluronic
Substance
Sorbitol
Acid Flavor
F127 Silicone
Solution
Saccharin
IFF **101**
Carrageenan
in % 1500 in %
in % in % in % in %
40.4 24.3 10 1.0 10.0 ---
45.0 22.7 15 1.0. . .
DETD TABLE IX

(percent by weight)
Surfactant
Coating Flavor SnF.sub.2
Fluronic
Substance
Polyol/SnF.sub.2
Acid IFF Concentration
F127 Silicone
Solution
Saccharin
101 Carrageenan
Silica
Antioxidants
in melt-emulsion
In % 1500 in %
in % in % in %
in % in %
in. . .
DETD The **release** of the SnF.sub.2 preparations from the floss of the invention subgingivally and interproximally in combination with the unique mechanical action. . . .
DETD . . . gingivitis is a localized condition that is responsive to treatment with the stabilized SnF.sub.2 floss of the present invention. The **release** of stabilized SnF.sub.2 preparations into "localized" inflammations and gingival eruptions delivers higher concentrations of SnF.sub.2 and imicrobial interproximally than achievable with. . . .
DETD . . . surfaces with the SnF.sub.2 floss of the present invention are proposed. The resultant efficient delivery of SnF.sub.2 in the preparation **released** from the floss; coupled with the mechanical cleaning of localized tooth surfaces promises superior antimries olinical effectiveness.
DETD TABLE X

L57 ANSWER 65 OF 79 USPATFULL on STN (Continued)
in % in % in %
in % in %
xn. . .
CLM What is claimed is:
. . . the cleaning preparation; ii. said interproximal delivery system splays upon being worked between interproximal surfaces; iii. said interproximal delivery system **releases** from between about 10 and about 80% by weight of said cleaning preparation upon splaying; and iv. said cleaning preparation. . . .
CLM What is claimed is:
4. The interproximal delivery system of claim 1, wherein the active chemotherapeutic agent is **released** during flossing at a rate between about 10% and about 80% by weight of said load.

CLM What is claimed is:
. . . into the floss at a rate between about 20 and about 50 mg/yd and wherein said additional splaying supportive preparation **releases** at a rate between about 30% and about 70% by weight of the load.

L57 ANSWER 66 OF 79 USPATFULL on STN
ACCESSION NUMBER: 87:12295 USPATFULL
TITLE: Method of treating the oral cavity with dental floss containing chemotherapeutic agents
INVENTOR(S): Hull, Ira, Clay Ct., Locust, NJ, United States 07760
White, Robert D., 65 Glen Gray Rd., Oakland, NJ, United States 07436

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4699711		19920724	<--
APPLICATION INFO.:	US 1987-45829		19890128 (7)	<--
DISCLAIMER DATE:	20070724			
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1988-270161, filed on 14 Nov 1988, now abandoned And a continuation-in-part of Ser. No. US 1988-270162, filed on 14 Nov 1988, now abandoned And a continuation-in-part of Ser. No. US 1988-270164, filed on 14 Nov 1988, now abandoned And a continuation-in-part of Ser. No. US 1988-270166, filed on 14 Nov 1988, now abandoned And a continuation-in-part of Ser. No. US 1988-270353, filed on 14 Nov 1988, now abandoned And a continuation-in-part of Ser. No. US 1988-270562, filed on 14 Nov 1988, now patented, Pat. No. US 4911927			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Rose, Shep K.			
LEGAL REPRESENTATIVE:	Lunek, Ernest V.			
NUMBER OF CLAIMS:	13			
EXEMPLARY CLAIM:	1			
LINE COUNT:	2222			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed is a method of treating the oral cavity with a surfactant, silicone, and chemotherapeutic agent containing preparation **released** from dental floss to alter local microbial ecology including: plaque formation, gingivitis and S. mutans count.

SUMM Ira Hill & Robert White Ser. No. 07/270,135 Filed Nov. 14, 1988 DENTAL FLOSS WITH **POLYVINYL** PYROLIDONE COMPLEX OF IODINE now, abandoned; . . . & Robert White Ser. No. 07/270,164 Filed: Nov. 14, 1988 METHOD OF TREATING THE ORAL CAVITY WITH DENTAL FLOSS CONTAINING **POLYVINYL** PYROLIDONE IODINE COMPLEX, now abandoned; . . . **released** from the floss, and

SUMM (3) Ser. No. 07/270,164--Filed Nov. 14, 1988, entitled Method of Treating the Oral Cavity with Dental Floss Containing **Polyvinyl**

L57 ANSWER 66 OF 79 USPATFULL on STN (Continued)
with flosses sold today. . . . flosses of the present invention. . .

SUMM Additionally, the floss of the present invention can contain therapeutic substances for **release** at concentrations up to 40 mg/yd. When these substances are included in the floss, they are **released** onto those interproximal and subgingival sites which cannot be reached by rinsing or brushing. This integral delivery system of substances in these concentrations is unique, in that it improves plaque control and gingivitis scores over other dental floss.

SUMM a. chemical cleansing with surfactants **released** from the floss of the present invention,

SUMM b. prolonged modification of the surface chemistry of the microflora by the coating materials **released**, e.g., silicones, **released** from the floss, and

SUMM c. alteration of microflora with various active ingredients contained in the load and **released** during flossing.

SUMM b. abrasive, disruption with abrasives **released** from floss including: silica, alkali-ium phosphates, calcium salts, at concentrations up to 40 mg/yd; and

SUMM c surfactant disruption resulting from the **release** of surfactants during flossing.

SUMM a. chemical cleansing with surfactants **released** from the floss,

SUMM c. alteration of the plaque with various active ingredients contained in the load and **released** during flossing including: tetrasodium pyrophosphate, tetrapotassium pyrophosphate etc.

SUMM b. abrasive removal by the abrasives **released** from the floss including: silica,dialcium phosphate, pyrophosphates etc., and

SUMM c. cleansing resulting from the **release** of surfactants during flossing.

SUMM . . . for "stain-off". Most dental caries implicate plaque in the formulation of caries, or tooth decay. In addition, these embedded bacteria **release** toxins that cause gingivitis, bleeding and swelling of the gums. Gingivitis can lead to periodontitis in which gums recede, pockets . . . and tartar control and have little access to the critical interproximal area. In contrast, the floss of the present invention **releases** substances interproximally and subgingivally. Additionally, some of these preparations such as mouth rinses and prerinses contain various antimicrobial substances which . . .

SUMM . . . concentrations; considering that the compositions of the present invention are not soluble in the mouth. Secondly, floss as treated will "**release**" these compositions during flossing and chemically cleanse the area of plaque and plaque precursors, bacteria, etc., while coating teeth and gum surfaces with a plaque matrix disrupting substance. The effects of these substances is particularly effective in disrupting, for prolonged periods, the plaque matrix on these interproximal sites. The cleaning that results from the compositions **released** from the floss also takes place on those interproximal surfaces brushing does not reach. This chemical cleansing and matrix disruption. . .

DETD R retain various flavors, sweeteners and **pharmacologically** preparations active on surfaces of the mouth imparting an unexpected prolonged effect of the **pharmacologically** active substances as well as prolonged flavor perception, and

DETD Furthermore, the cleaner, coating substance, and saliva or gingival crevice fluid mixture obtained when the compositions are **released** in the mouth are ingestible and can be pleasantly swallowed, which further

L57 ANSWER 66 OF 79 USPATFULL on STN (Continued)
Pyrollidone Iodine Complex, now abandoned;

SUMM . . . containing chemotherapeutic agents, e.g., antimicrobials, antibiotics, antioxidants, desensitizers, and anti-caries agents, such as tetracycline, chlorhexidine, sodium fluoride, stannous fluoride, and **polyvinyl** pyrollidone iodine complex with iodine.

SUMM The present invention is based upon the discovery that this type of mechanical action can be supplemented by the **release** of surfactants from the floss into the interproximal region. These **released** surfactants are readily solubilized in saliva and interproximal fluids to produce a detersive effect in the interproximal region during flossing. . .

SUMM (2) Ser. No. 07/270,135--filed Nov. 14, 1988, entitled Dental Floss with **Polyvinyl** Pyrollidone Complex of Iodine, now abandoned;

SUMM . . . and follow the contours of the teeth during flossing/cleaning. This improved mechanical cleaning is further supplemented with various insoluble abrasives **released** interproximally from the floss during flossing. This combination of abrasive, surfactant and mechanical action

is more efficient than mechanical action. . .

SUMM . . . the floss is positioned between teeth, the pressure applied during flossing. When the floss is slipped, the loaded substances are **released** and continue to be **released** during the sawing motion of flossing. This **releasing** action supplements the cleaning action of flossing by **releasing** cleaners to work with the floss.

SUMM 111. said interproximal delivery system **releases** from between about 12 and about 80% by weight of said cleaning preparation upon splaying; and

SUMM 1. Rapid **release** of substantial quantities of said soluble surfactant, silicone and abrasive when the floss is pulled across tooth surfaces. The construction. . . of unbonded floss, the absence of wax

and a unique loading process which encourages the floss to open up and **release** the load during flossing.

SUMM With the advent of "loading active ingredients" into floss for **release** during flossing as discussed below, the opportunity is available to include desensitizing agents into the load for release during flossing pain.

. . . desensitizing agents such as strontium chloride are used in dentifrices for "sensitive" teeth. These substances produce a comparable effect when **released** interproximally from the floss of the present invention. This desensitizing effect further improves the overall hedonics of the floss of.

SUMM This spreading out during flossing, also triggers the **release** mechanism which discharges most of the load interproximally during flossing, i.e., up to about 80% by weight. The surfactant/silicone/abrasive mixture thus, **released** is readily solubilized in the saliva and other fluids present. This solubilized mixture responds to the separate mechanical action of . . . **Release** of the load leaves gaps in the floss that tend to take up and hold some of the microscopic substances.

SUMM Up to about 80% of this load is **released** interproximal and subgingival sites during flossing, i.e., up to about 64 mg/yd. This **release** of surfactant cleansing in the area flossed is not evaluated

L57 ANSWER 66 OF 79 USPATFULL on STN (Continued)
distinguishes it from typical oral rinsing compositions used. . . the mouth with foam and can be pleasantly swallowed which is necessary for those flosses loaded with substantial quantities of **retainable** materials.

DETD The compositions **released** from the floss during flossing can disrupt plaque formation without resort to antimicrobial ingredients. The various surfaces of teeth and gums are contacted with a smooth thin film **released** from the floss which disrupts plaque formation. These coatings remain in the interdental spaces, between gum pockets and prolong this.

DETD . . . Thus, the floss may additionally comprise one or more chemotherapeutic agents, for example, tetracycline, chlorhexidine, sodium fluoride, stannous fluoride, and/or **polyvinyl** pyrollidone iodine complex, to mention but a few. Given the teachings of this disclosure, the skilled artisan will readily be. . .

DETD The preferred floss used in the method of the present invention is unique in its capacity to **release** its substances interproximally. Unexpectedly, the property of **releasing** these compositions correlates well to the coating and/or saturating of the treated floss strands during flossing. This tendency of the. . . the preferred loaded floss used in the method of the present invention, opens up tends to conform to surfaces and **releases** the loaded substances. Conversely, saturating floss, this **release** mechanism results in:

DETD 2. the floss strands continuing to **release** the loaded substances during flossing as the floss is moved over teeth, under the gun line and over the interproximal.

DETD Thus, the **release** mechanism of the preferred floss allows the floss to reach the interproximal sites and physically remove plaque, while at the same time **releasing** the compositions contained therein interproximally to assist in cleaning and/or treating these interproximal sites. This **releasing** of the compositions was quantified as follows:

DETD . . . of floss were again dried at 104 F for two hours and reweighed.

DETD The average quantity of loaded active ingredients **released** was established at 26 mg/yd with a significant variation between individuals or between pieces of floss.

DETD . . . containing various antimicrobial substances offers the opportunity to disrupt subgingival microflora and limit regrowth while also controlling supragingival plaque. The **released** supragingival and subgingivally of substantive chemotherapeutic antimicrobials and the plaque disrupting compositions from the preferred floss of the. . .

DETD Surprisingly, the cleaning/coating compositions **released** during the action of the present invention are good surface active properties and are able to clear the interproximal areas.

DETD 2. The treated floss **releases** the compositions contained therein/thereon onto surfaces of teeth and gums more effectively cleaning the interproximal sites.

DETD 3). The **released** compositions condition teeth and gums and leave the mouth feeling exceptionally clean and smooth. The surfaces of the teeth are. . . prolonged flavor perception is generally described as "freshness" and is stronger, more natural tasting and persists much longer with the **released** compositions than when stats-of-the-art, encapsulated "flavored" flosses are used under comparable conditions.

DETD . . . longer-than-expected time period thus enhancing the "its working" perception without negative "dirty mouth" connotations due to

L57 ANSWER 66 OF 79 USPATFULL on STN (Continued)
the bad taste of **released** plaque and debris. The latter is found to
DETD . to be beneficial towards plaque control and are included in the
compositions of this invention. See, for example, Segal, J. **Pharm.** Sci., 74:79-81 (1985) and Makimen, J. Am. Dent. Assoc., 111:740-741 (1985). . . .
DETD . . . and not commonly used in floss, can be selected from natural and synthetic gums such as: carrageenan, gum tragacanth, methyl **cellulose** and derivatives there of such as hydroxyethyl methyl **cellulose, polyvinyl** pyrrolidone, and hydrophilic carboxyvinyl polymers such as those sold under the trademark Carbopol 974.
DETD . . . or wax to floss do not provide for the quantity of loud required for the present invention nor the "controlled **release**" of this loaded material interproximally during flossing. Those processes used for waxing, for example, primarily coat the outer surfaces of. . .
DETD . . . to from between about 30 mg and about 300 mg per yard of floss.
These loaded substances are then controllably **released** into the oral cavity during flossing as from between about 10 and about 90% of the load. For example, a floss containing 60 mg/yd of loud will **release** between about 20 and about 32 mg of loud during flossing. Note, the rate
of **release** of these loaded active ingredients is easily controlled by varying the floss construction, the process of loading, and the composition. . . .
DETD . . . careful examination, primarily "coating". Thus, the pressures and forces encountered during flossing allow for the loaded material to be progressively **released** interproximally between the teeth and under the gum line. This "interstitial loading" is particularly critical in order to avoid "stripping". . . .
DETD . . . worked through the contact point and moved gently under the cuticle the loaded substances in the preferred floss are continually **released** into those areas where plaque and debris are difficult to clean and where irritation bleeding and bacterial infection tend to. . .
DETD . . . all these Examples the surfactant used was Pluronic F 127, the coating composition Dow Corning Silicone 1500, the Flavor IFF **101. Carrageenan** was included in the loading composition in all examples. The results are set out in Table III below.
DETD . . . GLYCERINE/
FLAVOR (ml) OTHER
SILICONE SACCHARIN SORBITOL ADDITIVES

EXAMPLE	in g.	in g.	in g	in g	FLOSS TYPE RESULTS
5	10.8/7.2	0/1.	3.5/2	**Carrageenan** 0.5	Unwaxed nylon Dusting dramatically improves mouth feel (pre-gelled)

L57 ANSWER 66 OF 79 USPATFULL on STN (Continued)
Saccharin
IFF **101**
Carrageenan
Silica
Propyl Gallate
salt, or Iodine

F 127 in %
1500 in %
in % in % in % in %. . .
DETD . . . about 60 mg/yd to about 10 mg/yd, the pathogenic microflora of infected sites can generally be controlled. Generally, the tetracycline **released** for each interproximal surface flossed is between about 1 mg and about 10 mg, with total **release** for all 60 surfaces requiring at least about 64 mg/yd.
DETD

Surfactant							
Coating Substance							
Sorbitol							
Acid	Flavor						
Pluronic							
Silicone Solution							
Saccharin							
IFF **101**							
Carrageenan							
F127 in %							
1500 in %							
48.4	24.3	15	1.0	10.0	--		
48.0	22.7	15.	. . .				

DETD TABLE IX

(percent by weight)

Surfactant			
Coating Substance			
Polyol/SnF.sub.2			
Acid	Flavor	SnF.sub.2	Concentra-
Pluronic			
Silicone Solution			
Saccharin			
IFF **101**			
Carrageenan			
Silica			
Antioxidants			
F127 in %			tion in melt-
1500 in %			
in %	in %	in %	in %

DETD The **release** of the SnF.sub.2 preparations from the floss of the invention subgingivally and interproximally in combination with the unique mechanical action. . . .
DETD . . . has been observed that gingivitis is a localized condition that
is responsive to treatment with the stabilized SnF.sub.2 floss. The **release** of stabilized SnF.sub.2 preparations into "localized"

L57 ANSWER 66 OF 79 USPATFULL on STN (Continued)
6 15.8/7.2 0/1. 5/2 **Carrageenan** 5
Unwaxed nylon
Improves mouth feel
powder
7 39.7/16.8
0/2.66 **19**.6/4.7 **Carrageenan** 1.77
Unwaxed nylon
Note in loading there
pre gelled plus was a single pass thru
powder to dry the chamber. Load was
250 mg/25 yd dry to
0/2.66 touch.
8 39.7/16.8
19.6/4.7 **Carrageenan** 1.77
Unwaxed poly-
Load was 2000 mg/25 yd
pre gelled plus ester 150/60/4
Dry to touch.
powder to dry

DETD TABLE V

EX-	COATING	EGRESITOL	CARRAGEENAN	DICALCIUM PHOSPHATE
AMPLE	CLEANER (%)	COMPOSITION (%)	(%)	VISCOSIFIER (%) DENTAL ABRASIVE FLAVOR
4Q	PEG Stearate/	Silicone glycol/2Q	10 10	15 5

. . .
DETD In contrast, when the **polyvinyl** pyrollidone iodine complex is included in the preparations loaded into the preferred floss for the present invention, the effect on. . . .
DETD The **polyvinyl** pyrollidone iodine complex is a stable, effective antimicrobial with minimal staining that is ideally suited for addition to the preferred. . . .
DETD 2. The required amount of **polyvinyl** pyrrolidone-iodine complex is added with vigorous mixing to achieve full dispersion, then immediately.
DETD TABLE VII

Surfactant			
Coating Substance	Flavor	Antioxidants	
		Iodine, Iodine	
Pluronic			
Silicone Sorbitol			

L57 ANSWER 66 OF 79 USPATFULL on STN (Continued)
inflammations and gingival eruptions delivers higher concentrations of SnF.sub.2 antimicrobial interproximally than achievable with. . .
DETD . . . localized to specific tooth surfaces with the SnF.sub.2 floss are proposed. The resultant efficient delivery of SnF.sub.2 in the preparation **released** from the floss coupled with the mechanical cleaning of localized tooth surfaces promises superior antiaries clinical effectiveness.
DETD TABLE X

	Sorbitol			(percent by weight)
Surfactant				
Coating Substance				
Polyol/SnF.sub.2				
Acid	Flavor	Antioxidants		
		SnF.sub.2		
Pluronic		Concentra-		
Silicone Solution				
Saccharin				
IFF **101**				
Carrageenan				
Silica				
Propyl Gallate				
F127 in %				tion in melt-
1500 in %				
in %	in %	in %	in %	in. . .

DETD . . . is expected that the long dodecene chain could be expected to influence substantivity and retention in the oral cavity. Controlled **release** of the free base chlorhexidine is expected which in turn is substantive to the teeth and gums (a primary requirement. . . .
DETD TABLE XI

				Chlorhexidine
Surfactant				
Coating Substance		Flavor		Concentration
Pluronic				
Silicone Chlorhexidine				
Saccharin				
IFF **101**				
Carrageenan				
Silica				
Sorbitol				
F127 in %				in melt-evolsion
1500 in %				
compound (2)				
in %	in %	in %	in. . .	

DETD TABLE XII

Surfactant			
Coating Substance			
Sorbitol NaF.sub.2			
	Flavor	Antioxidants	
		NaF.sub.2	
		Concentration	
Pluronic			
Silicone Solution			

L57 ANSWER 66 OF 79 USPATFULL on STN (Continued)
Saccharin
IFF **101**
Carrageenan
Silica
Propyl Gallate
in melt-emulsion
F127 in %
1500 in %
in % in % in % in % in %
. .
CLM What is claimed is:
. . . and binding agents; ii. said interproximal delivery system splays upon being worked between interproximal surfaces; iii. said interproximal delivery system **release** from between about 10 and about 80% by weight of said cleaning preparation upon splaying; and iv. said cleaning preparation;. . .
CLM What is claimed is:
2. A method of **releasing** interproximally, supragingivally and subgingivally a chemotherapeutic preparation from a dental floss containing an ingestible, oral hygiene cleaning preparation comprising: a.. . .
CLM What is claimed is:
. . . preparation is loaded into the floss at a rate between about 20 and about 50 mg/yd and wherein said preparation **releases** at a rate between about 30% and about 70% by weight of the load.

CLM What is claimed is:
. . . siloxane, and c. an active chemotherapeutic agent selected from the group consisting of tetracycline, chlorhexidine, stannous fluoride, sodium fluoride, and **polyvinyl** pyrrolidone iodine complex (PVPI), at a concentration from between about 0.5% to about 10.0% by weight of said preparation; wherein. . .
CLM What is claimed is:
. . . siloxane, and c. an active chemotherapeutic agent selected from the group consisting of tetracycline, chlorhexidine, stannous fluoride, sodium fluoride, and **polyvinyl** pyrrolidone iodine complex (PVPI), at a concentration from between about 0.55 to about 10.0% by weight of said preparation; wherein. . .
CLM What is claimed is:
. . . siloxane, and c. an active chemotherapeutic agent selected from the group consisting of tetracycline, chlorhexidine, stannous fluoride, sodium fluoride, and **polyvinyl** pyrrolidone iodine complex (PVPI), at a concentration from between about 0.5% to about 10.0% by weight of said preparation; wherein. . .
CLM What is claimed is:
. . . siloxane, and c. an active chemotherapeutic agent selected from the group consisting of tetracycline, chlorhexidine, stannous fluoride, sodium fluoride, and **polyvinyl** pyrrolidone iodine complex (PVPI), at a concentration from between about 0.5% to about 10.0% by weight of said preparation; wherein. . .
CLM What is claimed is:
. . . siloxane, and c. an active chemotherapeutic agent selected from the group consisting of tetracycline, chlorhexidine, stannous fluoride, sodium fluoride, and **polyvinyl** pyrrolidone iodine complex (PVPI), at a

L57 ANSWER 66 OF 79 USPATFULL on STN (Continued)
concentration from between about 0.5% to about 10.0% by weight of said preparation; wherein. . .

L57 ANSWER 67 OF 79 USPATFULL on STN
ACCESSION NUMBER: 91:86557 USPATFULL
TITLE: Zinc compound delivery system with improved taste and texture
INVENTOR(S): Cherukuri, Subraman R., Towaco, NJ, United States
Chau, Tommy L., Bridgewater, NJ, United States
PATENT ASSIGNEE(S): Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5059416		19911022	<--
APPLICATION INFO.:	US 1989-372394		19890626 (7)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Webman, Edward J.
LEGAL REPRESENTATIVE: Scola, Jr., Daniel A., Bell, Craig M.
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 737
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A new delivery system for zinc compounds and the process for its preparation is disclosed, which has use in a variety of products including comestibles such as chewing gum compositions, confections, **pharmaceuticals**, food products such as vitamin preparations, dentifrice compositions and throat lozenges. More particularly, this invention relates to a process for preparing a zinc compound delivery system comprised of a zinc core material coated with a first hydrophilic coating comprising a hydrocolloid material and a second hydrophobic coating selected from the group consisting of fats, waxes and mixtures thereof. The delivery system provides enhanced masking of the bitter flavor characteristic of zinc compounds, as well as reduced grittiness with retained stability at the elevated temperatures of product formulation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . its preparation is disclosed, which has use in a variety of products including comestibles such as chewing gum compositions, confections, **pharmaceuticals**, food products such as vitamin preparations, dentifrice compositions and throat lozenges. More particularly, this invention relates to a process for. . .
SUMM . . . to Cea et al. discloses solid particles of aspartame encapsulated by a coating material selected from the group consisting of **cellulose**, **cellulose** derivatives, arabinogalactin, gum arabic, polyolefins, waxes, vinyl polymers, gelatin, zein and mixtures thereof, wherein the amount of said coating material. . .
SUMM . . . nitrates, sulfates and chromates; and organic compounds such as the gluconates, acetates, tartrates and salicylates. Hydrocolloid materials include pectins, alginates, **cellulose** and its derivatives, gelatin, gums, mucilages, and mixtures. The gelatin used herein possesses a bloom strength on the order of. . .
SUMM . . . system may be incorporated into a variety of foods and

L57 ANSWER 67 OF 79 USPATFULL on STN (Continued)
confections, including chewing gums and hard candies, as well as **pharmaceutical** and nutritional preparations, as a deodorant in oral rinses, in tooth pastes and in throat lozenges. The present invention therefore includes chewing gums and hard candies, **pharmaceutical** and personal hygiene products such as dentifrices and mouthwashes, and nutritional supplements, all incorporating the present zinc compound delivery system.
SUMM It is a still further object of the present invention to provide **pharmaceutical** products, nutritional supplements, personal hygiene, confectionery and comestible products, all having contained therein the zinc compound delivery system of the. . .
DETD . . . gum arabic, tragacanth, karaya, ghatti, agar, alginates, carrageenans, fuercellaran, psyllium, and mixtures thereof. The hydrocolloid may also be selected from **polyvinyl** pyrrolidone, gelatin, dextran, xanthan, **cellulose**, **methylcellulose**, **ethylcellulose**, hydroxyethyl **cellulose**, hydroxypropyl **cellulose**, hydroxypropyl **methylcellulose**, carboxymethyl **cellulose**, low methoxy pectin, propylene glycol alginate, and mixtures thereof.
DETD . . . can be adjusted to accommodate a particular desired release rate and mouthfeel, depending on the vehicle, e.g., chewing gum, confection, **pharmaceutical**, oral preparation or dentifrice, in which it is incorporated. The core material can include a wide variety of materials such. . .
DETD . . . be incorporated in a number of ingestible products such as confections and the like, as well as chewing gum compositions, **pharmaceutical** preparations and denture products.
DETD . . . such as chicle, jelutong, gutta percha and crown gum. Synthetic elastomers such as butadiene-styrene copolymers, isobutylene-isoprene copolymers, polyethylene, polyisobutylene and **polyvinylacetate** and mixtures thereof are particularly useful.
DETD . . . a toothpaste, the dental vehicle contains as a solid portion, a gelling agent. The gelling agent includes alkali metal carboxymethyl **cellulose**, carrageenans such as viscarin and i-carrageenan, gelatin, starch, glucose, sucrose, **polyvinyl** pyrollidone, **polyvinyl** alcohol, gums such as gum tragacanth and gum karaya, hydroxypropyl **cellulose**, methyl **cellulose**, carboxyethyl **cellulose**, sodium alginate, synthetic inorganic complex silicate clays and magnesium aluminum silicate gel, as well as mixtures thereof. The solid portion or gelling agent of the vehicle is typically present in amount of about 0.25-10% by weight. Alkali metal carboxymethyl **cellulose** includes the lithium, sodium and potassium salts. Sodium carboxymethyl **cellulose** is preferred.
CLM What is claimed is:
10. The delivery system of claim 8 wherein said hydrocolloid is selected from the group consisting of **polyvinyl** pyrrolidone, gelatin, dextran, xanthan, curdan, **cellulose**, **methylcellulose**, **ethylcellulose**, hydroxyethyl **cellulose**, hydroxypropyl **cellulose**, hydroxypropyl **methylcellulose**, carboxymethyl **cellulose**, low methoxy pectin, propylene glycol alginate, and mixtures thereof.

IT Gums and Mucilages
IT Cottonseed oil
IT Fats, biological studies
IT Fatty acids, biological studies
IT Gelatins, biological studies

L57 ANSWER 67 OF 79 USPATFULL on STN (Continued)
IT Glycerides, biological studies
IT Palm oil
IT Rape oil
IT Safflower oil
IT Soybean oil
IT Sunflower oil
IT Waxes and Wax substances
(coating materials containing, for zinc **pharmaceuticals**)
IT Chewing gum
IT Confectionery
IT Dentifrices
IT Mouthwashes
IT **Pharmaceutical** dosage forms
(lozenges containing, taste-masking compns. for)
IT **Pharmaceutical** dosage forms
(oral, of zinc compds., hydrocolloid and waxy coating materials for)
IT Oils, glyceridic
(palm kernel, coating materials containing, for zinc **pharmaceuticals**)
IT Oils, glyceridic
(rice bran, coating materials containing, for zinc **pharmaceuticals**)
IT 10-70-4D, Sorbitol, sates 8063-14-9, Papillum 9000-01-5, Gum arabic 9000-28-6, Gum ghatti 9000-36-6, Karaya gum 9000-65-1, Gum tragacanth 9000-69-5, Pectin 9025-18-0, Agar 9002-18-0, **Polyvinyl** pyrrolidone 9003-39-8, **Cellulose** 9004-34-6, **Cellulose**, biological studies 9004-36-8, Dextran, biological studies 9004-54-0, Hydroxypropyl **cellulose** 9004-65-3, Hydroxypropyl methyl **cellulose** 9005-32-7D, Alginic acid, derivs. 9025-37-0, Propylene glycol alginate 11138-66-2, Xanthan gum 25618-55-7D, Polyglycerol, esters 54724-00-4, Candelilla (**coating** materials containing, for zinc **pharmaceuticals**)
IT 546-46-3, Zinc citrate 557-34-6, Zinc acetate 557-41-5, Zinc formate 1332-26-1, Zinc glycerol phosphate 1314-13-2, Zinc oxide, biological studies 1330-43-4D 4468-02-4, Zinc gluconate 6228-53-1, Zinc succinate 7440-66-6D, Zinc, compds. 7646-85-7, Zinc chloride, biological studies 7699-45-8, Zinc bromide 7733-02-0, Zinc sulfate 7779-88-6, Zinc nitrate 7779-90-2, Zinc phosphate 7783-24-6 7783-49-5, Zinc fluoride 10139-47-6, Zinc iodide 13530-65-9, Zinc chromate 13773-83-6, Zinc dithionate 16283-36-6, Zinc salicylate 16871-71-9, Zinc fluosilicate 17949-65-4, Zinc pivalate 30949-56-5 36393-20-1, Zinc aspartate 60388-02-5 121837-45-6, Zinc ascorbate (**pharmaceuticals** containing, coating materials for)
IT **9000-07-1D**, Carrageenan, derivs.
(**coating** materials containing, for zinc **pharmaceuticals**)

L57 ANSWER 68 OF 79 USPATFULL on STN
ACCESSION NUMBER: 90:23427 USPATFULL
TITLE: Method and apparatus for adding chemotherapeutic agents
to dental floss
INVENTOR(S): Hill, Ira D., Clay Ct., Locust, NJ, United States 07760
White, Robert D., 65 Glen Gray Rd., Oakland, NJ, United States 07436

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4911927		19900327	<--
APPLICATION INFO.:	US 1988-270562		19881114 (7)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Page, Thurman K.			
LEGAL REPRESENTATIVE:	Limek, Ernest V.			
NUMBER OF CLAIMS:	17			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	6 Drawing Figure(s); 3 Drawing Page(s)			
LINE COUNT:	1559			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and apparatus for the manufacture of various dental flosses containing chemotherapeutic preparations which are **releasable** during flossing.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and apparatus for the manufacture of various dental flosses containing chemotherapeutic preparations which are **releasable** during flossing.

SUM4 . . . up and down motion". It has now been found that this type of mechanical action can be supplemented by the **release** of surfactants from the floss into the interproximal region. These **released** surfactants are readily solubilized in saliva and interproximal fluids to produce a detersive effect in the interproximal region during flossing. .

SUM4 . . . and follow the contours of the teeth during flossing/cleaning. This improved mechanical cleaning is further supplemented with various insoluble abrasives **released** interproximally from the floss during flossing. This combination of abrasive, surfactant and mechanical action

SUM4 is more efficient than mechanical action.

SUM4 1. Rapid **release** of substantial quantities of saliva soluble surfactant, silicone and abrasive when the floss is pulled across tooth surfaces. The construction . . . of unbonded fibers, the absence of wax

SUM4 and a unique loading process which encourages the floss to open up and **release** the load during flossing.

SUM4 With the advent of "leading active" into floss for **release** during flossing as discussed below, the opportunity is available to include desensitizing agents into the load to minimize flossing pain. . .

L57 ANSWER 68 OF 79 USPATFULL on STN (Continued)
when desensitizing agents such as strontium chloride are used in dentifrices for "sensitive" teeth. These substances produce a comparable effect

released interproximally from the floss of the invention. This effect is considered to be a combination of the effects of the floss of the . .

SUM4 This spreading out during flossing, also triggers the **release** mechanism which discharges most of the load interproximally during flossing, i.e. up to about 80% by weight. The surfactant/silicone/abrasive mixture thus, **released** is readily solubilized in the saliva and other fluids present. This solubilized mixture responds to the separate mechanical action of . .

SUM4 **Release** of the load interproximally in the floss which tends to take up and hold some of the microscopic substances. . .

SUM4 . . . to about 80 percent by weight, thus cleaning and plaque fighting formulation. Up to about 80% of this load is **released** onto interproximal and subgingival sites during flossing, i.e. up to about 64

mg/yd. This **release** of surfactant cleansing in the area flossed is not available with flosses sold today. The flosses of the invention show. .

SUM4 Additionally, the floss of the invention can contain therapeutic substances for **release** at concentrations up to 40 mg/yd. When these substances are included in the load they are **released** onto those interproximal and subgingival sites which cannot be reached by rinsing or brushing. This interproximal **release** of substances in these concentrations is unique, improves plaque control and gingivitis scores and as described in more detail in. .

SUM4 a. chemical cleansing with surfactants **released** from the floss of the invention,

SUM4 b. prolonged modification of the surface chemistry of the microfloras by the coating materials **released**, e.g. silicones, **released** from the floss, and

SUM4 c. alteration of microflora with various actives contained in the load and **released** during flossing.

SUM4 b. abrasive disruption of abrasives **released** from floss including: silica, dicalcium phosphate, pyrophosphates etc, at concentrations up to

40 mg/yd; and

SUM4 c. surfactant disruption resulting from the **release** of surfactants during flossing.

SUM4 a. chemical cleansing with surfactants **released** from the floss,

SUM4 c. alteration of the plaque with various actives contained in the load and **released** during flossing including: tetrasodium pyrophosphate, tetrapotassium pyrophosphate etc.

SUM4 b abrasive removal by the abrasives **released** from the floss including: silica, dicalcium phosphate, pyrophosphates etc, and

SUM4 c cleansing resulting from the **release** of surfactants during flossing.

SUM4 . . . for "mischief". Most dental texts implicate plaque in the formation of caries, or tooth decay. In addition, these embedded bacteria **release** toxins that cause gingivitis, bleeding and swelling of the gums. Gingivitis can lead to periodontitis in which gums recede, pockets . . .

SUM4 . . . and tartar control and have little access to the critical interproximal areas. In contrast, the floss of the present invention **releases** substances interproximally and subgingivally. Additionally,

L57 ANSWER 68 OF 79 USPATFULL on STN (Continued)
some of these preparations such as mouth rinses and prerinses contain various antimicrobial substances which.

SUM4 . . . high concentrations; considering that the compositions of the invention are not soluble in the floss. Secondly, floss as treated will **release** these compositions during flossing and chemically cleanse the area of plaque and plaque precursors, bacteria, etc., while coating

teeth and gum surfaces with a plaque matrix disrupting substance. The **release** of these substances from the floss is effective in disrupting, for prolonged periods, the plaque matrix on these interproximal sites. The cleansing that results . . . compositions **released** from the floss also takes place on those interproximal surfaces brushing does not

reach. This chemical cleansing and matrix disruption.

SUM4 1. certain various flavors, sweeteners and **pharmacologically** preparations active on surfaces of the mouth imparting an unexpected prolonged effect of the **pharmacologically** active substances as well as prolonged flavor perception, and

SUM4 . . . mouth, is novel. Furthermore, the cleaner, coating substance, and saliva or gingival crevice fluid mixture obtained when the compositions are **released** in the mouth are ingestible and can be pleasantly swallowed, which further distinguishes it from typical oral cleaning compositions used. . . . the mouth with foam and can be pleasantly swallowed which is necessary for those flosses loaded with substantial quantities of **releasable** materials.

SUM4 The compositions **released** from the floss during flossing can disrupt plaque formation with respect to antimicrobial ingredients. The various surfaces of teeth and gums are coated with a smooth thin film **released** from the floss which disrupts plaque formation. These coatings remain in the interdental spaces for extended periods and prolong this.

SUM4 The floss of the present invention is unique in its capacity to **release** the "loaded" composition of the invention interproximally. Unexpectedly, the property of **releasing** these compositions correlates with the opening up and/or flattening of the treated floss strands during flossing. This tendency of the . . .

SUM4 . . . damaging delicate gum tissue. In contrast, the loaded floss of the invention, upon such bends and abrasion to surfaces and **releases** the loaded substances interproximally during flossing. This **release** mechanism results in:

SUM4 3. the floss strands continuing to **release** the loaded substances during flossing as the floss is moved over teeth, under the gum line and

over the interproximal. . . .

SUM4 Thus, the **release** mechanism of the floss of the present invention allows the floss to reach the subgingival sites and physically remove plaque, while at the same time **releasing** the compositions of the invention interproximally to assist in cleaning and/or treating these interproximal sites. This **releasing** of the compositions was quantified as follows:

SUM4 . . . types of floss were again dried at 104° F. for two hours and reweighed. The average quantity of loaded actives **released** was established at 26 mg/yd with no significant variation between individuals or between pieces of floss.

SUM4 . . . containing various antimicrobial substances offers the opportunity to disrupt subgingival microflora and limit regrowth while also controlling supragingival plaque. The **release** interproximally and subgingivally of substantive chemotherapeutic antimicrobials and the

L57 ANSWER 68 OF 79 USPATFULL on STN (Continued)
plaque disrupting compounds of the invention from the floss of the.

SUM94 Surprisingly, the cleaning/coating compositions **released** from the floss of the present invention retain good surface active properties and
are able to clear the interproximal areas. . .
SUM94 2. The treated floss **releases** the compositions of the invention onto surfaces of teeth and gums more effectively cleansing the interproximal sites.
SUM94 3. The **released** compositions condition teeth and gums and leaves the mouth feeling exceptionally clean and smooth. The surfaces of the teeth are . . . prolonged flavor perception is generally described as "freshness" and is stronger, more natural tasting and persists much longer with the **released** compositions of the present invention than when state-of-the-art, encapsulated "flavored" flosses are used under comparable conditions.
SUM94 . . . longer-than-expected time period thus enhancing the "its working" perception without negative "dirty mouth" connotations due to the bad taste of **released** plaque and debris. The latter is found to reduce frequency of use and undermine the regular cleansing advantage. The feeling. . .
SUM94 . . . and not commonly used in floss, can be selected from natural and synthetic gums such as: carrageenan, gum tragacanth, methyl **cellulose** and derivatives there of such as hydroxyethyl methyl **cellulose, polyvinyl** pyrrolidone, and hydrophylic carboxyvinyl polymers such as those sold under the trademark Carbopol 934. Generally,
about 0.01 percent to about. . .
SUM94 . . . or wax to floss do not provide for the quantity of load required for the present invention nor the "controlled **release**" of this loaded material interproximally during flossing. These processes used for waxing, for example, primarily coat the outer surfaces of. . .
SUM94 . . . to from between about 10 mg and about 100 mg per yard of floss.
These loaded substances are then controllably **released** into the oral cavity during flossing at from between about 10 and about 80% of the load. For example, a floss containing 60 mg/yd of load will **release** between about 20 and about 32 mg of load during flossing. Note, the rate
of **release** of these loaded actives is easily controlled by varying the floss construction, the process of loading, and the composition of. . .
SUM94 . . . careful examination, primarily "coating". Thus, the pressures and forces encountered during flossing allow for the loaded material to be progressively **released** interproximally between the teeth and under the gum line. This "interstitial loading" is particularly critical in order to avoid "stripping". . . .
SUM94 . . . is worked through the contact point and moved gently under the sumline the loaded substances of the invention are continually **released** into those areas where plaque and debris are difficult to clean and where irritation bleeding and bacterial infection tend to. . .
SUM94 . . . all these Examples the sufatsant used was Pluronic F 127, the

L57 ANSWER 68 OF 79 USPATFULL on STN (Continued)
10 10. . .
SUM94 . . . fibers in each instance be twisted into a floss construction which is suitable for receiving the various loads and for **releasing** substantial portions of this load during flossing.
DET2 The pressures and forces encountered during flossing result in the loaded material being progressively, **released** interproximally between the teeth and under the gum line. This "interstitial loading" is particularly critical inorder to avoid "stripping" the. . . is worked
through the contact point and moved gently under the sumline the loaded substances of the invention are continually **released** into those areas where plaque and debris are difficult to clean and where irritation bleeding and bacterial infection tend to.
DET2 . . . 'flavor oils" or wax do not provide for the quantity of load achieved by the present invention nor the "controlled **release**" of this loaded material interproximally during flossing. Those processes used for waxing, for example, primarily coat the outer surfaces of. . .
DET2 . . . the floss range from about 10 mg to about 80 mg per yard of floss. These loaded substances are then controllably **released** into the oral cavity during flossing at from between about 10 and about 80 percent by weight of the load. For example, a floss containing 40 mg/yd of load will **release** between about 20 and about 32 mg/yd of load during flossing. As noted above, the rate of **release** of these loaded actives is controlled by the floss construction, the process of loading,
and the preparation of the loaded.
DET2 . . . The dramatic effect of floss construction on loading the preparations of the invention are set forth in Table VII. The **release** rate of these loaded preparations were similar to those described previously.
CLM What is claimed is:
. . . between about 10 and about 80 mg of said preparation are contained in
one yard of said floss in a **releasable** state.

CLM What is claimed is:
3. A method of adding a chemotherapeutic preparation to dental floss according to claim 1 wherein said preparation is **released** during flossing at a rate between about 10% and about 80% by weight of said load.

CLM What is claimed is:
. . . and contained in the interstitial spaces between the fibers of said floss such that up to 80% by weight is **released** from said floss during flossing.

CLM What is claimed is:
. . . preparation is loaded into the floss at a rate between about 20 and about 50 mg/yd and wherein said preparation **releases** at a rate between about 30% and about 70% by weight of the load.

L57 ANSWER 69 OF 79 USPATFULL on STN (Continued)
coating composition Dow Corning Silicone 7500, the Flavor IFF 101. **Carrageenan** was included in the loading composition in all examples. The results are set out in Table III below.

SUM94						. . . GLYCERINE/	
			FLAVOR (ml)				
			OTHER				
	SILICONE SACCHARIN						
			SORBITOL				
			ADDITIVES				
EXAMPLE							
	in g.	in g.	in g.	in g	FLOSS TYPE		
						RESULTS	
5	10.8/7.2	0/1.	3.5/2		**Carrageenan** 0.5		
					Unwaxed nylon		
						Darting dramatically	
					(pre-selled)	improves mouth feel	
6	15.8/7.2	0/1.	0/2		**Carrageenan** ?		
					Unwaxed nylon		
					powder	Improves mouth feel	
7	39.7/16.8						
		0/2.66	19.6/4.7		**Carrageenan** 1.77		
					Unwaxed nylon		
						Wax is loading there	
					pre selled plus	was a single pass thru	
					powder to dry	the chamber. Load was	
						250 mg/25 yd dry to	
						touch.	
8	39.7/16.8						
		-/2.66	19.6/4.7				
					Carrageenan 1.77		
					Oriented poly-		
						Load was 2000mg/25 yd	
					pre selled plus		
					ester 150/68/4		
						Dry to touch.	
					powder to dry		

SUM94 TABLE V

	COATING	CARRAGEENAN		
EX-	COMPOSITION	VISCOSITY		
			DICALCIUM PHOSPHATE	
				FLAVOR
AMPLE				
	CLEANER (%)			
	(%)	SORBITOL (%)		
		(%)	DENTAL ABRASIVE	
				(%)
40	PEG Stearate			
	Silicone glycol/20			

L57 ANSWER 70 OF 79 USPAT2 on STN
ACCESSION NUMBER: 2005:170726 USPAT2
TITLE: Preparation of a granule containing protein, corn starch and sugar layered on an inert particle
INVENTOR(S): Becker, Nathaniel T., Hillsborough, CA, UNITED STATES
Green, Thomas E., Montara, CA, UNITED STATES
PATENT ASSIGNEE(S): Genencor International, Inc., Rochester, NY, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 7300779	B2	20071127
APPLICATION INFO.:	US 2004-939576		20040913 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2002-190785, filed on 25 Jun 2002, Pat. No. US 6790643 Continuation of Ser. No. US 1999-428153, filed on 27 Oct 1999, Pat. No. US 6413749		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-105674P	19981027 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Marx, David M.	
LEGAL REPRESENTATIVE:	Jacobson, Jill A.	
NUMBER OF CLAIMS:	13	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	524	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Granules that include a protein core are described. The protein core includes a protein matrix which includes a protein mixed together with a
starch. The protein matrix can be layered over a seed particle or the protein core can be homogeneous. The protein can be an enzyme or a therapeutic protein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM94 Proteins such as **pharmaceutically** important proteins like hormones and industrially important proteins like enzymes are becoming more widely used. Enzymes are used in several.
SUM94 U.S. Pat. No. 4,106,991 describes an ungraved formulation of enzyme granules by including within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-10% w/w based on the dry weight of the whole composition. In addition, this patent. . .
SUM94 . . . diatomaceous earth or sodium citrate crystals. The film forming
material may be a fatty acid ester, an alkorylated alcohol, a **polyvnyl** alcohol or a ethorylated alkylphenol.
SUM94 . . . perboate or sodium percarbonate. Accomplishing all these desired characteristics simultaneously is a particularly challenging task since, for example, hary delayed **release** or low-dust agents such as fibrous **cellulose** or kaolin leave behind insoluble residues
DET2 . . . between the seed particle and the matrix or the matrix and the barrier layer, for example, a coating such as **polyvnyl** alcohol (PVA)
DET2 Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as

L57 ANSWER 69 OF 79 USPAT2 on STN (Continued)
enzymes.
DETD ... more synthetic polymers or other excipients as known to those skilled in the art. Suitable synthetic polymers include polyethylene oxide, **polyvinyl** alcohol, **polyvinyl** pyrrolidone, polyethylene glycol and polyethylene oxide/polypropylene oxide.
DETD Suitable coatings include water soluble or water dispersible film-forming polymers such as **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, gum arabic, xanthan, **carrageenan**, chitosan, latex polymers, and enteric polymers. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.
DETD ... Preferably, the outer coating layer comprises partially hydrolyzed PVA having low molecular weight vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVA-methylmethacrylate copolymer and PVP-PVA copolymer.
DETD ... . . . coupertially coated with 92.6 kg of an aqueous solution containing 7.1 kg (6.2% w/w) titanium dioxide, 2.9 kg (2.5% w/w) **methylcellulose**, 2.9 kg (2.5%) Purecote B790, 1.2 kg (1.5% w/w) Neodol 23/6.5, and 2.0 kg (1.6% w/w) of polyethylene glycol at. . .
CLM What is claimed is:
. . . fluid bed coater to form a barrier layer around the admixture layer; and d) spraying an outer coating selected from **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan, and **carrageenan** into the fluid bed **coater** until an outer coating is formed around the barrier layer.

L57 ANSWER 70 OF 79 USPAT2 on STN
ACCESSION NUMBER: 2004:239812 USPAT2
TITLE: Process for coating solid particles
INVENTOR(S): Chaubey, Kaul J., Midland, MI, UNITED STATES
Keary, Colin M., Midland, MI, UNITED STATES
PATENT ASSIGNEE(S): Dow Global Technologies,Inc., Midland, MI, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 7070829	B2	20060704
	WO 2005020247		20050303
APPLICATION INFO.:	US 2002-464525		20020823 (10)
	WO 2002-US26764		20020823
			19940621 PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-317402P	20010904 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Michener, Jennifer	
NUMBER OF CLAIMS:	17	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	479	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process for coating solid particles which comprises the steps of a) contacting a gas with a fluid composition comprising 1) a polymer and ii) a liquid diluent to produce a foam, and b) contacting the produced foam with solid particles and agitating the particles to provide a coating on the solid particles.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUM1 This invention relates to a process for coating solid particles, particularly drug-containing solid particles, such as **pharmaceutical** tablets, granules and pellets.
SUM2 Coatings are generally applied to solid particles, such as **pharmaceutical** forms, to protect the ingredients against the atmosphere, to mask unpleasant tastes, to make tablets easier to swallowing, to improve.
SUM4 **Methylcellulose** and hydroxypropyl **methylcellulose** have been used for a long time as coating materials for **pharmaceutical** forms. U.S. Pat. No. 3,451,130 discloses that these coating are tacky, uneven, and require extensive polishing after coating. To solve . . . ethanol, from 35 to 45 weight percent of chloroform and from 2 to 5 weight percent of low viscosity methyl **cellulose**. Since the issue of the U.S. patent, the coating technology has progressed and high quality coatings are obtainable without the use of chloroform. Nowadays **methylcellulose** and hydroxypropyl **methylcellulose** are dissolved in water or a mixture of water and alcohol and sprayed on an agitated mass of **pharmaceutical** forms. The spraying technique is a sophisticated process which requires well-defined processing parameters and quite complex equipment
Moreover,

L57 ANSWER 70 OF 79 USPAT2 on STN (Continued)
the viscosity of the solutions of **methylcellulose** and hydroxypropyl **methylcellulose** must be low enough that they are still sprayable.
SUM6 U.S. Pat. No. 3,607,864 discusses in detail the disadvantages of spray coating of **pharmaceutical** solid forms, such as the high pressures which are required to sufficiently atomize a coating medium. To solve these problems, U.S. Pat. No. 3,607,364 discloses a process for coating a **pharmaceutical** solid form wherein a foamed viscous sugar medium is applied to the solid surface, the coating medium is then urged. . . .
DETD . . . ghatti, guar gum, exudate gums, seaweed gums, seed gums, microbial gums, carrageenan, dextran, gelatin, alginates, pectins, starches, polysaccharides, and the **cellulose** ethers or **cellulose** esters, starch derivatives, guar derivatives or xanthan derivatives. Starch derivatives, guar derivatives or xanthan derivatives are described in more detail.
DETD Preferred polymers are **cellulose** esters or **cellulose** ethers. Preferred **cellulose** esters are carboxy-C.sub.1-C.sub.3-alkyl **cellulose**s, such as carboxymethyl **cellulose**s, carboxy-C.sub.1-C.sub.3-alkyl hydroxy-C.sub.1-C.sub.3-alkyl **cellulose**s, such as carboxymethyl hydroxyethyl **cellulose**s. Preferably, the **cellulose** ethers are C.sub.1-C.sub.3-alkyl **cellulose**s, such as **methylcellulose**s, C.sub.1-C.sub.3-alkyl hydroxy-C.sub.1-3-alkyl **cellulose**s, such as hydroxyethyl **methylcellulose**s, hydroxypropyl **methylcellulose** or ethyl hydroxyethyl **cellulose**; hydroxy-C.sub.1-3-alkyl **cellulose**s, such as hydroxyethyl **cellulose** or hydroxypropyl **cellulose**; mixed hydroxy-C.sub.1-C.sub.3-alkyl **cellulose**s, such as hydroxyethyl hydroxypropyl **cellulose**; or alkylhydroxyalkyl hydroxypropyl **cellulose**s, the alkoxy group being straight-chain or branched and containing 2 to 8 carbon atoms. Most preferably, the fluid composition comprises a water-soluble **cellulose** ether, such as a **methylcellulose** with a methyl molar substitution of from 0.5 to 2.0, preferably from 1 to 2.5, or a hydroxypropyl **methylcellulose** with a MS.sub.methoxyl of from 0.5 to 2.0, preferably from 1.0 to 2.5 and a MS.sub.hydroxypropoxyl of from 0.05 to 2.0, preferably from 0.1 to 1.5. The viscosity of the **methylcellulose** ether generally is from 1 to 100,000 mPa.multidot.s, preferably from 10 to 10,000 mPa.multidot.s, more preferably from 3 to 5,000.
DETD Generally polymers if used are chosen which have surface-active properties. The above-mentioned polymers, particularly water-soluble **cellulose** ethers, are useful as a surfactant in a water-based fluid composition used in step a) of the process of the. . .
DETD . . . viscous due to the presence of the polymer. In case the fluid film comprises a hydrophilic polymer such as a **cellulose** ether, water is retained in the lamellae of the gas bubbles. The drainage of the liquid from the lamellae is . . . foam qualities can be achieved, particularly if the polymer i) in fluid composition comprises a polymer for producing the foam is a **cellulose** ether. The foam quality FQ is given in percent at atmospheric pressure and 25.degree. C. and is defined as follows:
. . .
DETD . . . The process of the present invention is particularly useful for
coating solid particles containing a drug, that means for solid **pharmaceutical** forms, preferably tablets, granules, pellets, caplets, capsules, lozenges, suppositories, pessaries and implantable dosage forms. The solid particles may comprise known ingredients, such as **pharmaceutical** excipients, for example lactose, dicalcium phosphate, microcrystalline **cellulose**, sugars, minerals, **cellulose** powder, disintegrants, binders, lubricants, colorants, flavorants or

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combinations thereof.
DETD . . . the present invention. All parts and percentages are by weight unless otherwise indicated. The ethyl and hydroxyethyl substitutions of the **cellulose** ethers indicated in the examples below are measured and calculated according to ASTM D3876. The apparent viscosities indicated in the.
DETD Placebo tablets are produced from 20 weight percent of a microcrystalline **cellulose**, which is commercially available from FMC Corporation under the trademark Avicel PH-101, 74.5 weight percent of fast flow lactose, commercially available from DMV International **Pharma** and Foremost Farms USA under the designation FT-324, and 0.5 weight percent of magnesium stearate. The composition is compressed into. . .
DETD . . . percent of a powder composition in 95 weight percent of water is prepared. The powder composition comprises a hydroxypropyl methyl **cellulose** and is commercially available under the Trademark Opadry Yellow (YS-81172), manufactured by Colorcon (West Point, Pa., USA). From the aqueous. . .
CLM What is claimed is:
. . . weight average molecular weight of at least 10,000 and is one or more
polymers selected from the group consisting of **cellulose** ethers, **cellulose** esters, polyalkylene oxides, homo- and copolymers of vinyl alcohol, and homo- and copolymers of vinylpyrrolidone, wherein the liquid diluent is. . .
CLM What is claimed is:
5. The process of claim 3 wherein the polymer i) is a C.sub.1-C.sub.3-alkyl **cellulose**, a C.sub.1-C.sub.3-alkyl hydroxy-C.sub.1-3-alkyl **cellulose** or a hydroxy-C.sub.1-3-alkyl **cellulose** or a homo- or copolymers of vinylpyrrolidone or polyethylene oxide.
CLM What is claimed is:
7. The process of claim 6 wherein the polymer i) is a C.sub.1-C.sub.3-alkyl **cellulose**, a C.sub.1-C.sub.3-alkyl hydroxy C.sub.1-3-alkyl **cellulose** or a hydroxy-C.sub.1-3-alkyl **cellulose** or a homo- or copolymers of vinylpyrrolidone or polyethylene oxide
CLM What is claimed is:
8. The process of claim 7 wherein the polymer i) is a methyl **cellulose** with a methyl molar substitution DS.sub.methoxyl of from 0.05 to 3.0 or a hydroxypropyl **methylcellulose** with a DS.sub.methoxyl of from 0.5 to 3.0 or a MS.sub.hydroxypropoxyl of from 0.05 to 2.0.
CLM What is claimed is:
11. The process of claim 1 wherein the polymer i) is a C.sub.1-C.sub.3-alkyl **cellulose**, a C.sub.1-C.sub.3-alkyl hydroxy-C.sub.1-3-alkyl **cellulose** or a hydroxy-C.sub.1-3-alkyl **cellulose** or a homo- or copolymers of vinylpyrrolidone or polyethylene oxide.
CLM What is claimed is:
12. The process of claim 11 wherein the polymer i) is methyl **cellulose** with a methyl molar substitution MS.sub.methoxyl of from 0.5 to 2.0 and

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a ME.sub.hydroxypropyl of from 0.05 to 2.0.

CLM What is claimed is:
. . . comprise a drug, wherein the polymer i) has a weight average molecular weight of at least 10,000 and is a **cellulose** ether or a **cellulose** ester and wherein the amount of other additives, if present, is up to 25 weight percent, based upon the total...
IT 9000-65-1, Gum arabic 9000-07-1, Carrageenan 9000-28-6, Gum ghatti 9000-30-0, Guar gum 9000-36-6, Karaya gum 9000-65-1, Gum tragacanth 9002-49-1, Pectin 9004-34-6D, **Cellulose**, esters 9004-34-6D, **Cellulose**, ethers 9004-54-0, Dextran, biological studies 9004-65-3, Hydroxypropyl methyl **cellulose** 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 11138-66-2, Xanthan gum
(**coating** of solid drug particles with polymeric foams)
IT **9000-07-1**, Carrageenan
(**coating** of solid drug particles with polymeric foams)

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at least one of a strengthening polymer or a plasticizer. The coatings of the present invention can be applied to **pharmaceutical**, including neutraceutical, and veterinary solid dosage forms, confectionery, seeds,
animal feed, fertilizers, pesticide tablets and granules, and foods, are
readily . . . media, and, when applied as a coating and ingested by, for example, a human, do not significantly retard or extend **release** of active ingredient(s) from a substrate coated therewith.
SUMM It is a common practice to coat **pharmaceutical** and veterinary tablets to obtain several advantages. Among these are to mask unpleasant tasting
active ingredients with a barrier coat, . . .
SUMM Another very important function of a **pharmaceutical** or veterinary tablet coating is to improve the integrity of the tablet itself. Uncoated tablets are often subject to being.
SUMM Currently, most commercially available coatings utilize a synthetic **cellulosic** polymer such as **hydroxypropylmethylcellulose** (HPMC). Other synthetic film-formers which are commonly used include **ethylcellulose, methylcellulose, polyvinylpyrrolidone**, and polyvinyl acetate. These coating materials may be used alone or in combination with secondary film-formers such as sodium alginate or.
. . .
SUMM . . . proportion to the increase in disintegration time. Many other agents commonly used in coating compositions are also known to delay **release** of **pharmaceutical** agents, such as enteric coatings which use polymeric film forming materials which are insoluble in water, or gastric fluid, some of these being specifically selected to by-pass both
the stomach and small intestine and provide colonic **release**.
SUMM The coatings of this invention meet U.S. **Pharmacopoeia** standards for rapid or immediate dissolution (U.S.P. monograph 23) of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates. They do not adversely impact or retard **release** of active ingredients from a substrate coated with them. Further, the coatings of this invention are readily removed and rapidly . . .
SUMM . . . with the present invention by a coating composition which comprises a unique combination of materials specifically adapted for a prompt **release** when placed aqueous media or ingested, e.g., by a human. The coating composition of the present invention comprises microcrystalline **cellulose**, carrageenan, and at least one of a strengthening polymer and a plasticizer. More specifically, the present invention provides a prompt **release**, edible, hardenable **coating** composition comprising microcrystalline **cellulose** and **carrageenan**, and at least one of strengthening polymer or plasticizer, preferably both, as well as to dry coatings and aqueous dispersions.
SUMM The present invention also provides **pharmaceutical**, including neutraceutical, and veterinary solid dosage forms, confectionery, seeds,
animal feed, fertilizers, pesticide tablets and granules, and foods coated with the prompt **release** edible, hardenable composition of this invention.
SUMM . . . application, the term "edible" is intended to mean food grade materials which are approved by regulatory authorities for use in **pharmaceutical** or food applications. The term "hardenable" used to describe the coating compositions of this invention is intended to

L57 ANSWER 71 OF 79 USPAT2 on STN
ACCESSION NUMBER: 2003:23368 USPAT2
TITLE: Edible coating composition
INVENTOR(S): Augello, Michael, Marlboro, NJ, United States
Dell, Sheila M., New Hope, PA, United States
Tsason, Domingo C., Bensalem, PA, United States
Modliszewski, James J., Brick, NJ, United States
Fuisz, Richard C., Rochessin, DE, United States
Werner, David E., West Grove, PA, United States
PATENT ASSIGNEE(S): FMC Corporation, Philadelphia, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6709713	B2	20040323
APPLICATION INFO.:	US 2002-165022		20020607 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2000-471706, filed on 27 Jan 2000, now patented, Pat. No. US 6432440		

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-119005P	19990208 (60)	<--
	US 1999-139782P	19990507 (60)	<--
	US 1999-162514P	19991029 (60)	<--
	US 1999-167407P	19991124 (60)	<--
	US 1999-172526P	19991217 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Pulliam, Amy
LEGAL REPRESENTATIVE: Woodcock Washburn LLP
NUMBER OF CLAIMS: 62
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 1470
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable **coating** composition containing microcrystalline **cellulose** and **carrageenan** and either a strengthening polymer, a plasticizer or both. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable **coating** composition containing microcrystalline **cellulose** and **carrageenan** and either a strengthening polymer, a plasticizer or both. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

SUMM This invention relates to edible, hardenable, prompt **release coating** compositions comprising microcrystalline **cellulose, carrageenan** and

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include only . . . that can be hardened packaged but which do not resist abrasive forces significantly. The terms "immediate", "rapid" or "prompt" **release** as applied to dissolution rates of tablets or the coating compositions of this invention or tablets coated with the compositions of this invention mean that the coatings of this invention
meet U.S. **Pharmacopoeia** standards (U.S.P. monograph 23) for rapid or immediate dissolution of active ingredients from tablets or other solid dosage forms coated therewith. They provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates. They do not, consistent with the **pharmacopeia** standards above, when placed in aqueous media or ingested by, e.g., a human, significantly impact or retard **release** or dissolution of tablets or other solid dosage forms coated therewith. For example, when a **pharmaceutical** solid dosage form is coated with the coating of this invention and ingested by a human or other animal, the . . .
SUMM The microcrystalline **cellulose**, either coprocessed with carrageenan or simply blended therewith, interacts with the carrageenan to provide important film-forming characteristics required to provide an elegant coating which is particularly useful in, for example, coating **pharmaceutical** and veterinary tablets, caplets, granules, and spheres which contain active ingredients which require **release** promptly after being placed in aqueous media or ingested.
SUMM Microcrystalline **cellulose** is a purified, partially depolymerized **cellulose** that is generally produced by treating a source of **cellulose**, preferably alpha **cellulose** in the form of a pulp from fibrous plants, with a mineral acid, preferably hydrochloric acid. The acid selectively attacks the less ordered regions of the **cellulose** polymer chain, thereby exposing and freeing the crystallite sites, forming the crystalline aggregates which constitute microcrystalline **cellulose**. These are then separated from the reaction mixture and washed to remove degraded by-products. The resulting wet mass, generally
containing 40 to 60 percent moisture, is referred to in the art by several names, including hydrolyzed **cellulose**, microcrystalline **cellulose**, microcrystalline **cellulose** wetcake, or simply wetcake. The microcrystalline **cellulose** that can be used as dried or may be further modified, for example, by attrition and/or drying, and utilized as
SUMM Microcrystalline **cellulose** may also be produced for use in the present invention using a steam explosion treatment. In this process, wood chips
SUMM or other **cellulosic** materials are placed in a chamber into which super-heated steam is introduced. After being maintained for a period of
about 1-5 minutes, the exit valve is opened rapidly, releasing the contents explosively and yielding microcrystalline **cellulose**. No additional acid need be introduced into the reaction mixture, since it is believed that the acidic materials in the wood chips and the elevated
temperature and pressure hydrolyze the **cellulose** and degrade it. In addition to the specific forms of microcrystalline **cellulose**, the present invention also contemplates the use of other **cellulose** derivatives, including microreticulated **cellulose**, also known as microreticulated microcrystalline **cellulose**, and powdered **cellulose**

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such as a commercial material sold as "Solka Floc®.".

SUMM As discussed in greater detail below, the microcrystalline **cellulose** preferred for use in the present invention is microcrystalline **cellulose** which has an average particle size below about 100 microns, preferably microcrystalline **cellulose** which been attrited or has an average particle size in the range of 1 to 50 microns, preferably 1 to.

SUMM Carrageenan is used in combination with microcrystalline **cellulose** to form the elegant prompt **release coatings** of the present invention. **Carrageenan** for use in the present invention is a naturally derived carrageenan, including the grades further defined below as iota,

kappa, . . . sulfate content of iota carrageenan may range from about 25% to 34%, preferably about 30%. Kappa is suitable because **carrageenan** which has a **25%** ester sulfate content and lambda carrageenan which has a 35% ester sulfate content. The sodium salt of iot. carrageenan is. . . Iota carrageenan require heating water to different temperatures to dissolve. The iota carrageenans which are

suitable for the microcrystalline **cellulose**/iota carrageenan material of this invention are soluble in water heated up to 90° C. (176° F.). Preferred grade of Iota

SUMM The microcrystalline **cellulose** and carrageenan may be coprocessed or may be blended in any suitable manner, such as dry blending.

SUMM Coprocessed microcrystalline **cellulose**/Iota carrageenan is rapidly peptizable. Peptization means that the agent can readily be dispersed in water in a colloidal state. . . . be dispersed [peptized]

in a colloidal state with minimal agitation. Thus, the novel coating formulations in which the coprocessed microcrystalline **cellulose**/Iota carrageenan is incorporated can be hydrated in as little as 0.5 hour, but more preferably peptized in 1 to 3 hours. . .

SUMM The coprocessed microcrystalline/iota carrageenan compositions useful in

this invention may be prepared by first stirring hydrolyzed **cellulose** wetcake, such that the agglomerate size of the wetcake particles is

generally not more than about 20 microns, preferably. . . at which the particular grade of iota carrageenan being used dissolves, adding the dry carrageenan to the microcrystalline **cellulose**, and then mixing the components, preferably homogenizing the mixture to assure ultimate mixing, and drying the mixture. Spray drying is normally used to. . .

SUMM . . . It is possible to prepare the coatings directly, that is, before the drying of the wetcake, from a dispersion of microcrystalline **cellulose** wetcake and the carrageenan by accounting for the water present in the wetcake and adding the other ingredients in the. . . coats for a dispersion would be less economical. Furthermore, drying by any method may enhance the association of the microcrystalline **cellulose** with the carrageenan which may result in a more satisfactory prompt **release** coating.

SUMM Dry blended microcrystalline **cellulose** (e.g., Avicel® PH-105, average particle size **20** microns) and iota **carrageenan**, has been found to provide **coating** compositions that are at least equal to, and

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maltodextrin, lactose, mannitol and other sugars. Of these, maltodextrin

and mannitol are preferred fillers. The prompt **release** coating compositions of the invention may include at least one surfactant. Such surfactants include either anionic or nonionic surfactants. Useful. . . .

SUMM . . . basis a preferred composition of this invention comprises at least about 42%, suitably about 45% to about 75% of microcrystalline **cellulose** and carrageenan, preferably carrageenan, about 45% to about 60%; about 0.5% to about 30% of strengthening polymer, more. . . .

SUMM . . . may be preferable to maintain agitation of the aqueous dispersion during the entire period of its being sprayed onto the **pharmaceutical** or veterinary solid dosage form, confectionary, seeds, animal feed, fertilizer, pesticide tablets, or food.

SUMM The preferred edible, hydrophilic prompt **release** coating formulations of this invention may generally be prepared and used according to a simple procedure. A dry blend of microcrystalline **cellulose**/carrageenan powder or a dry blend of microcrystalline **cellulose** and carrageenan, and a strengthening polymer, such as **hydroxyethylcellulose**, polyethylene glycol or other acceptable plasticizer, optionally together with solid fillers such as maltodextrin, lactose, mannitol or the like, . . .

SUMM In the formulations of microcrystalline **cellulose** and iota carrageenan, a simple propellent mixer provides adequate agitation for rapid hydration. The speed of hydration may be due to the thixotropic behavior of a formulation which sets up during overnight storage.

Unlike

coating formulations based primarily on hydroxyalkyl ethers of **cellulose**, for example, HPMC, sustained drying of the microcrystalline and carrageenan-based formulations of this invention does not need to be continued. . . .

SUMM . . . Engineering. Equipment variables which one skilled in the art can manipulate to provide an elegant coating based on the microcrystalline **cellulose** and carrageenan materials, either coprocessed or dry blended, include inlet temperature, outlet temperature, air flow, and rate of the spray of the. . .

SUMM **Hydroxyethylcellulose** binds water more effectively than carrageenan does. Thus, the presence of the major amount of carrageenan in the formulations of. . . the carrageenan which dilutes the negative effect of HEC on drying time. Thus, in the case of the active **pharmaceutical** agents, for example, ibuprofen, the outlet temperature can be reduced and still provide a product enough drying time to be commercially. . .

SUMM **Hydroxyethylcellulose** is particularly susceptible to clogging spray nozzles at high temperatures. An additional benefit provided by the formulations of this invention.

SUMM The level of coating applied to **pharmaceutical** or veterinary dosage forms is preferably between about 0.5% to about 4% by weight of the uncoated dosage form, more. . . .

SUMM . . . to those of the uncoated tablets used as a substrate for coating. This is an additional unexpected benefit of the **coatings** based on **carrageenan** and microcrystalline **cellulose**, and it differs from the known drawbacks of HPMC.

SUMM All components of the formulation are typically **pharmaceutically** acceptable, edible food grade materials.

DETD In a Patterson-Kelley turn shell blender were placed 14.43 grams of

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spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), **10.36** grams of **polyvinylpyrrolidone** 29/32 (GAF), 16.40 grams of polyethylene glycol 8000 (Union Carbide Corporation), and 0.2 grams of yellow #5 food color. After.

DETD By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), **0.25** gram of **hydroxyethylcellulose** (Aqualon® 250L, Hercules Incorporated), 10.40 grams of polyethylene glycol 8000, and 0.30 gram of

yellow #5 food color was added.

DETD By the method of Example 1, a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250L, Hercules Incorporated), 5.40 grams of polyethylene glycol 8000, 2.5 grams of Micro Talo, and 0.30 gram of red.

DETD By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), **0.25** gram of **hydroxyethylcellulose** (Aqualon® 250L, Hercules Incorporated), 10.40 grams of polyethylene glycol 8000, and 0.30 gram of

yellow #5 food color was added.

DETD By the method of **Example** 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 0.25 gram of **hydroxyethylcellulose** (Aqualon® 250L, Hercules Incorporated), 10.40 grams of polyethylene glycol 8000, 0.10 gram of yellow #5 food color, and 0.30 gram. . . . resulting viscous solution was sprayed using a Vector High Coater LDCS onto 1 Kg of corrs

comprised

of 20% microcrystalline **cellulose** and 80% calcium carbonate, each weighing on average 1.05 grams. Conditions used include an inlet temperature of 73-80° C., and.

DETD By the method of Example 1 a dry mixture of 19.05 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), **10.45** grams of polyethylene glycol 8000, and 0.30 gram of yellow #5 food color was added to 600 grams of deionized. . . stirred while it was sprayed using a Vector High Coater LDCS onto 1 Kg of the same cores of microcrystalline **cellulose** and calcium carbonate tablets that were mated in Example 5. Conditions used include an inlet temperature of 70-75° C., an outlet. . . . tablet weight gain of 3%. . . was less than 3 minutes. This coating was not as elegant as coatings containing **hydroxyethylcellulose**.

DETD By the method of Example 1 a dry mixture of 20.95 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 0.28 gram of **hydroxyethylcellulose** 250L, 11.40 grams of polyethylene glycol 8000, and 0.330 gram of yellow iron oxide was added to 450 grams of. . . solution was continuously stirred while it was sprayed using a Vector

High Coater LDCS onto 1.07 Kg of compressed microcrystalline **cellulose** cores (Avicel® PH-200) debossed with an FMC logo, each weighing on average 0.267 gram. Conditions used include an inlet temperature. . . .

DETD By the method of Example 1 a dry mixture of 285.75 grams of spray-dried,

coprocessed microcrystalline **cellulose**/iota **carrageenan** (90:10), 7.5 grams of **hydroxyethylcellulose** 250L, 156.0 grams of polyethylene glycol 8000, and 45.0 grams of hydrophilic red iron oxide was prepared. A portion (60. . . . have as elegant an appearance as those prepared in

L57 ANSWER 71 OF 79 USPAT2 on STN (Continued)
Examples 1 through 7 in which the 70:30 combination of microcrystalline **cellulose** and iota carrageenan was employed. Friability testing was satisfactory, but there was minor chipping and erosion observed for these coated.
DETD By the method of Example 1, a dry mixture of 184.8 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota carrageenan (70:30), 5.02 grams of **hydroxyethylcellulose** 250L, 304.2 grams of polyethylene glycol 8000, 1.25 grams of methyl paraben, 0.15 gram of propyl paraben, 10.48 grams of. . .
DETD By the method of Example 1 a dry mixture of 194.7 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota carrageenan (70:30), 5.61 grams of **hydroxyethylcellulose** 250L, 304.4 grams of polyethylene glycol 8000, 1.65 grams of methyl paraben, 0.165 gram of propyl paraben,
10.48 grams of. . .
DETD By the method of Example 1 a dry mixture of 68.94 grams of spray-dried, coprocessed microcrystalline **cellulose**/iota **carrageenan** (70:30), 1.02 gram of **hydroxyethylcellulose** 250L, 37.87 grams of polyethylene glycol 8000, 0.565 grams of methyl paraben, 0.0565 gram of propyl paraben, 10.28 grams of. . .
DETD In a Patterson-Kelley twin shell blender were placed 229.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 160.65 grams) and iota carrageenan (68.85 grams), 69.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 148.5 grams of polyethylene glycol 8000 (Union Carbide Corporation), 13.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation),. . .
DETD By the method of Example 12, a dry blend comprising 238.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 166.95 grams) and iota carrageenan (71.55 grams), 60.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 148.5 grams of polyethylene glycol 8000 (Union Carbide Corporation), 13.5 grams of maltodextrin (Maltrin M-180), and 9.0 grams. . . at 50 rpm, 900 ml. 0.05 M phosphate buffer at 30 minutes showed that 100**±**0.8% of the acetaminophen had been **released** at pH 5.8 and 97**±**2.2% of the ibuprofen had been **released** at pH 7.2. Dissolution testing using USP apparatus 1 (basket) at 50 rpm, 900 ml, 0.05 M acetate buffer, pH 4.5 showed that 93**±**2.9% of the aspirin had been **released**.
DETD By the method of Example 12, a dry blend comprising 238.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 166.95 grams) and iota carrageenan (71.55 grams), 60.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 148.5 grams of polyethylene glycol 8000 (Union Carbide Corporation), and 22.5 grams of maltodextrin (Maltrin M-180), was dispersed. . . . 90° C. Hydration required 75 minutes. A Accela-Cota coater was charged with 12 Kg of cores comprised of 20% microcrystalline **cellulose** and 80% calcium carbonate, each weighing on average 1.25 grams. The coater was operated at an inlet
temperature of 92.8-108.3°.
DETD In a Patterson-Kelley twin shell blender were placed 234.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 166.5 grams) and iota carrageenan (67.5 grams), 67.5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 63.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), 63.0 grams of titanium dioxide, and 22.5 grams of. . .

L57 ANSWER 71 OF 79 USPAT2 on STN (Continued)
glycol 8000 (Union Carbide Corporation), 10.19 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation), . . .
DETD In a Patterson-Kelley twin shell blender were placed 70.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**22.**5 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 1.5 gram of stearic acid. Simultaneously 37.5 grams of titanium dioxide was added to 1516.7 grams of. . .
DETD In a Patterson-Kelley twin shell blender were placed 300 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, **200** grams) and iota **carrageenan** (**100** grams) and 100 grams of polyethylene glycol 8000 (Union Carbide Corporation). After the dry components had been thoroughly blended, the entire blend was. . .
DETD In a Patterson-Kelley twin shell blender were placed 49.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 34.3 grams) and iota **carrageenan** (**14.**7 grams), **11.**0 grams of **hydroxyethylcellulose** (Aqualon® 250L), 33.0 grams of polyethylene glycol 8000 (Union Carbide Corporation), 7.0 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation), . . .
DETD In a Patterson-Kelley twin shell blender were placed 43.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 33 grams) and iota **carrageenan** (**10** grams), **20** grams of **hydroxyethylcellulose** (Aqualon® 250L), 23.0 grams of triacetin, 0.2 grams of propylene glycol alginate, and 3 grams of Pluronic F-68 (BASF). After. . .

Ingredient Amount (g)

Macrocrystalline **cellulose** 37.5
(Avicel PH-**105**)
Iota **carrageenan** **14.**7
Polyethylene glycol 8000 34
Hydroxyethylcellulose 250 L 11
Maltodextrin M-180 3
DETD

Example:
31 32 33
Weight (grams)

Avicel PH-105 38 34.3 34.3
Iota **carrageenan** **11** **14** **7** **14.**7
Hydroxyethylcellulose -- 11 11
PGA-sup.a
PEG-sup.b 34 33 33
Lecithin-sup.c 7 6 7
Maltrin M-180 3 3

sup.aPropylene glycol alginate (Protonal. . .
DETD

Weight (grams)

Avicel PH-105 33
Iota **carrageenan** 10
Hydroxyethylcellulose 20

L57 ANSWER 71 OF 79 USPAT2 on STN (Continued)
DETD In a Patterson-Kelley twin shell blender were placed 76.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**21.**0 grams), **22.**5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 28.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), 10.0 grams of Red #40 aluminum lake, and 0.7. . .
DETD In a Patterson-Kelley twin shell blender were placed 76.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**21.**0 grams), **22.**5 grams of **hydroxyethylcellulose** (Aqualon® 250L), 28.5 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), 10.0 grams of a red dye blend (Warner Jenkinson). . .
DETD In a large Patterson-Kelley twin shell blender were placed 1.940 Kg of a
blend of microcrystalline **cellulose** (Avicel® PH-105, 1.358 Kg) and iota carrageenan (0.582 Kg), 0.476 Kg of **hydroxyethylcellulose** (Aqualon® 250L), 0.277 Kg of maltodextrin (Maltrin® M-100, Grain Processing Corporation), and 1.307 Kg of polyethylene glycol 8000 (Union
Carbide. . .
DETD In a Patterson-Kelley twin shell blender were placed 72.00 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 56 .**25** grams) and iota **carrageenan** (**16.**55 grams), 33.00 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 4.35 grams of hydrophilic red iron oxide. After being thoroughly mixed, the dry components were added to. . .
DETD In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**18.**0 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), 35.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation), and 22.5 grams of hydrophilic yellow oxide. After being. . .
DETD In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**18.**0 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 21.0 grams of maltodextrin (Maltrin® M-180, Grain Processing Corporation). Simultaneously 22.5 grams of titanium dioxide was added. . .
DETD In a Patterson-Kelley twin shell blender were placed 73.5 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**18.**0 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 12.0 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation). Simultaneously 31.0 grams of titanium dioxide was added. . .
DETD In a Patterson-Kelley twin shell blender were placed 76.0 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 55.5 grams) and iota **carrageenan** (**22.**5 grams), 33.0 grams of **hydroxyethylcellulose** (Aqualon® 250L), and 7.0 grams of maltodextrin (Maltrin M-180, Grain Processing Corporation). Simultaneously 30.0 grams of titanium dioxide was added. . .
DETD In a Patterson-Kelley twin shell blender were placed 71.23 grams of a blend of microcrystalline **cellulose** (Avicel® PH-105, 49.94 grams) and iota **carrageenan** (**21.**39 grams), **16.**01 grams of **hydroxyethylcellulose** (Aqualon® 250L), 40.05 grams of polyethylene

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PGA-sup.a 4
Pluronic F-68 3

sup.aPropylene glycol alginate (Protonal® ester SD-LB, Pronova).
DETD

Ingredient Weight (grams)

Avicel PH-105 37
Iota **carrageenan** **14.**5
Hydroxyethylcellulose **22**
Mannitol.sup.a 15.5
Pluronic F-68 3
Blue Lake #2 8
Deionized water 1150
Reaction time 2.5
Caplets
Ibuprofen 1 kg
Acetaminophen.
DETD A dispersion of 9.30 grams of microcrystalline **cellulose** (Avicel® PH-102, FMC Corporation) and 20.7 grams of iota carrageenan (Viscarin® SD-389) in 1300 grams of deionized water was prepared.

CLM What is claimed is:
1. An edible, hardenable, prompt **release, pharmaceutical** and veterinary coating composition comprising a dry blend of (a) microcrystalline **cellulose** having an average particle size less than 100 microns, (b) a film forming amount of carrageenan, and (c) at least.

. . . polymer and a plasticizer, wherein said coating composition does not, when ingested or placed in an aqueous medium, significantly retard **release** of active ingredient from a pharmaceutical and veterinary solid dosage form to which said coating is applied.

CLM What is claimed is:
2. The coating composition of claim **1**, wherein the **carrageenan** is iota carrageenan.

CLM What is claimed is:
4. The coating composition of claim **3**, wherein said strengthening polymer is selected from the group consisting of **hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, ethylcellulose, methylcellulose,** and **polyvinylpyrrolidone**.

CLM What is claimed is:
5. The coating composition of claim **3**, wherein the strengthening polymer
is **hydroxyethylcellulose**.

CLM What is claimed is:
15. The coating composition of claim 1, wherein the weight ratio of microcrystalline **cellulose** to carrageenan is in the range of about 85:15 to about 65:35.

CLM What is claimed is:
16. The coating composition of claim 1, wherein the microcrystalline

L57 ANSWER 71 OF 79 USPAT2 on STN (Continued)
cellulose has an average particle size in the range of 1 to 50 microns.

CLM What is claimed is:
17. The coating composition of claim 16, wherein the microcrystalline **cellulose** has an average particle size in the range of about 1 to about 50 microns.

CLM What is claimed is:
19. An aqueous dispersion comprising a coating composition of the edible, hardenable, prompt **release** coating composition of claim 1.

CLM What is claimed is:
22. An aqueous dispersion of a composition of claim 1, 2, or 3, wherein said microcrystalline **cellulose** and carrageenan are present in a weight ratio of about 70:30; said strengthening polymer is selected from

the group consisting of **hydroxyethylcellulose**, **hydroxypropylmethylcellulose**, **methylcellulose**, **ethylcellulose**, **hydroxypropylcellulose** and **polyvinylpyrrolidone**; said plasticizer is selected from at least one of the group consisting of polyethylene glycol, triacetin, dibutyl sebacate, propylene glycol, . . .

CLM What is claimed is:
23. An aqueous dispersion of a composition of claim 19, wherein said microcrystalline **cellulose** and carrageenan are present in a weight ratio of about 70:30.

CLM What is claimed is:
24. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, high molecular weight polyethylene glycol and maltodextrin, wherein said microcrystalline **cellulose** has a particle size less than 50 microns.

CLM What is claimed is:
25. A **pharmaceutical** solid dosage form comprising the edible coating composition of claim 24.

CLM What is claimed is:
27. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxethylcellulose**, mannitol, a surfactant and a coloring agent, wherein said microcrystalline **cellulose** has a particle size less than 50 microns.

CLM What is claimed is:
28. A **pharmaceutical** solid dosage form comprising the edible coating composition of claim 27.

CLM What is claimed is:
30. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, and a coloring agent, wherein said microcrystalline **cellulose** has a particle size less than 50 microns.

CLM What is claimed is:
31. A **pharmaceutical** solid dosage form comprising the edible coating

L57 ANSWER 71 OF 79 USPAT2 on STN (Continued)
composition of claim 30.

CLM What is claimed is:
33. An edible, coating composition consisting of microcrystalline **cellulose**, iota carrageenan, **hydroxyethylcellulose**, high molecular weight polyethylene glycol and a coloring agent, wherein said microcrystalline **cellulose** has a particle size less than 50 microns.

CLM What is claimed is:
35. A dry **coating** composition comprising microcrystalline **cellulose**, **carrageenan** and at least one of a strengthening polymer and a plasticizer, wherein said dry composition can be hydrated in a. . .

CLM What is claimed is:
36. An edible, hardenable, prompt **release pharmaceutical** and veterinary coating composition comprising a dry blend of (a) microcrystalline **cellulose**, (b) a film forming amount of carrageenan, and (c) at least one of a strengthening polymer and a plasticizer, wherein said coating composition does not, when ingested or placed in an

aqueous medium, significantly retard **release** or active ingredients from a **pharmaceutical** and veterinary solid dosage form to which said coating is applied.

CLM What is claimed is:
37. A **pharmaceutical** and veterinary tablet coated with the coating composition of claim 36.

CLM What is claimed is:
38. A **pharmaceutical** and veterinary tablet coated with the coating composition of claim 1.

CLM What is claimed is:
40. A dry, edible, hardenable, prompt **release**, **pharmaceutical** and veterinary coating composition comprising (a) microcrystalline **cellulose**, (b) a film forming amount of carrageenan, and (c) at least one of a strengthening polymer and a plasticizer, wherein said coating composition does not, when ingested or placed in an aqueous medium, significantly retard **release** of active ingredients from a **pharmaceutical** and veterinary solid dosage form to which said coating is applied and wherein said microcrystalline **cellulose** and carrageenan are coprocessed.

CLM What is claimed is:
41. A **pharmaceutical** and veterinary solid dosage form coated with the coating composition of claim 40.

CLM What is claimed is:
42. A **pharmaceutical** and veterinary solid dosage form coated with the coating composition of claim 40 wherein the weight ratio of microcrystalline **cellulose** to **carrageenan** in the **coating** composition is in the range of about 90:10 to about 60:40.

L57 ANSWER 72 OF 79 USPAT2 on STN
ACCESSION NUMBER: 2002137415 USPAT2
TITLE: Granule containing enzyme, corn starch and sugar layered on an inert particle
INVENTOR(S): Becker, Nathaniel T., Hillsborough, CA, United States
Green, Thomas S., Montara, CA, United States
PATENT ASSIGNEE(S): Genencor International, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6790643	B2	20040914
APPLICATION INFO.:	US 2002-380785		20020625 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-428153, filed on 27 Oct 1999, now patented, Pat. No. US 6413749		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-105874P	19981027 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Naff, David M.	
LEGAL REPRESENTATIVE:	Genencor International, Inc.	
NUMBER OF CLAIMS:	19	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	526	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Granules that include a protein core are described. The protein core includes a protein matrix which includes a protein material together with a

starch and optionally sugar such as sucrose. The protein matrix can be layered over a seed particle or the protein more can be homogeneous. The

protein can be an enzyme or a therapeutic protein. A barrier layer may surround the protein core, and a coating can be applied to the seed particle, the protein matrix and/or the barrier layer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUM01 Proteins such as **pharmaceutically** important proteins like hormones and industrially important proteins like enzymes are becoming more widely used. Enzymes are used in detergent . . .
SUM02 U.S. Pat. No. 4,106,991 describes an improved formulation of enzyme granules by including within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-60% w/w based on the dry weight of the composition. In addition, this patent. . .
SUM03 . . . diatomaceous earth or sodium citrate crystals. The film forming

material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.
SUM04 . . . perborate or sodium percarbonate. Accomplishing all these desired characteristics simultaneously is a particularly challenging task since, for example, many delayed **release** or low-dost agents such as fibrous **cellulose** or kaolin leave behind insoluble residues.
SUM06 . . . between the seed particle and the matrix or the matrix and the barrier layer, for example, a coating such as **polyvinyl** alcohol (PVA).
SUM08 Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other

L57 ANSWER 72 OF 79 USPAT2 on STN (Continued)
therapeutic proteins and industrially important proteins such as enzymes.
SUM09 . . . more synthetic polymers or other excipients as known to those skilled in the art. Suitable synthetic polymers include polyethylene oxide, **polyvinyl** alcohol, **polyvinyl** pyrrolidone, polyethylene glycol and polyethylene oxide/polypropylene oxide.
SUM46 Suitable coatings include water soluble or water dispersible film-forming polymers such as **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, gum arabic, xanthan, **carrageenan**, chitosan, latex polymers, and enteric **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.
SUM48 Preferably, the outer coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVA-methylmethacrylate copolymer and PVP-PVA copolymer.
DET2 . . . commercially coated with 92.6 kg of an aqueous solution containing 7.3 kg (6.2% w/w) titanium dioxide, 2.9 kg (2.5% w/w) **methylcellulose**, 2.9 kg (2.5%) Puromote 8700, 1.2 kg (1.5% w/w) Neodol 23/6.5, and 2.0 kg (1.67% w/w) of polyethylene glycol at. . .
CLM What is claimed is:
6. The granule of claim 5 wherein the coating is selected from **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan and carrageenan.

CLM What is claimed is:
9. The granule of claim 5 wherein the coating is a **cellulose** derivative.

CLM What is claimed is:
16. The granule of claim 15 wherein the coating is selected from **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan and carrageenan.

CLM What is claimed is:
19. The granule of claim 15 wherein the coating is a **cellulose** derivative.

L57 ANSWER 73 OF 79 USPAT2 on STN
ACCESSION NUMBER: 2002:232102 USPAT2
TITLE: Lubricious coatings for substrates
INVENTOR(S): Worrall, Robert Edward, Sherwood Park, CANADA
Yin, Hua Qing, Sherwood Park, CANADA
Naylor, Antony George, Sherwood Park, CANADA
Hunkin, Peter Howard, Sherwood Park, CANADA
Cholowski, Walter Carlton Theodore, Edmonton, CANADA
Bowley, Leonard Selvin, Sherwood Park, CANADA
Field, David Jones, Edmonton, CANADA
PATENT ASSIGNEE(S): Hydrogel Pharmaceuticals Corp., Alberta, CANADA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6723350	B2	20040420
APPLICATION INFO.:	US 2001-791513		20020423 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2001-840637, filed on 23 Apr 2001		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-285884P	20010423 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Pak, John	
LEGAL REPRESENTATIVE:	Fish & Richardson P.C.	
NUMBER OF CLAIMS:	4	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	974	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides methods and kits to form water swellable gel coatings, preferably lubricious coatings, on substrates, and coated substrates thus formed. The coatings contain one or more antimicrobial metals formed with atomic disorder, together with one or more antimicrobial metals formed with atomic disorder such that the coatings provide an antimicrobial and anti-inflammatory effect when wet. The invention also provides a method to produce metal powders by sputtering a coating onto a moving surface, and then scraping the coating with one or more strippers to produce the metal powder. The method is particularly useful for producing large amounts of nanocrystalline antimicrobial metal powders formed with atomic disorder, useful in the water swellable gel coatings of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM= The lubricious polymer is preferably a hydrophilic polymer in powder form, most preferably one or more of carboxymethyl **cellulose**, **polyvinyl** alcohol and alginate. The antimicrobial metal is preferably one or more of Ag, Au, Pt or Pt (most preferably Ag).

SUM= '**Pharmaceutically**- or therapeutically-acceptable' is used herein to denote a substance which does not significantly interfere with the

L57 ANSWER 73 OF 79 USPAT2 on STN (Continued)
biological studies 9012-76-4, Chitosan 11138-66-2, Xanthan gum (lubricious **coatings** contg. nanocryst. silver and polymers for medical surfaces)
IT **9000-07-1**, Carrageenan
(lubricious **coatings** containing nanocryst. silver and polymers for medical surfaces)

L57 ANSWER 73 OF 79 USPAT2 on STN (Continued)
ACCESSION NUMBER: 2002:232097 USPAT2
TITLE: Edible PGA coating composition
INVENTOR(S): Kaplin, Michael, Williamsville, NY, UNITED STATES
PATENT ASSIGNEE(S): FMC Corporation, Philadelphia, PA, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6923861	B2	20050802
APPLICATION INFO.:	US 2002-77338		20020215 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2001-994252, filed on 26 Nov 2001, Pat. No. US 6699315, issued on 2 Mar 2004		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-2847789	20010215 (60) <--
	US 2001-2686089	20010214 (60) <--
	US 2000-2534069	20001128 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Brunsman, David	
LEGAL REPRESENTATIVE:	Woodcock Washburn LLP	
NUMBER OF CLAIMS:	12	
EXEMPLARY CLAIM:	8	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	717	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An edible, hardenable coating composition is disclosed which comprises high levels of low viscosity propylene glycol alginate and a surfactant, which may additionally contain a filler, a pigment and optionally a small amount of a secondary film former and/or a strengthening polymer. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . of a secondary film former and/or a strengthening polymer. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.

SUM= This invention relates to edible, hardenable prompt **release** coating compositions comprising a film forming amount of low viscosity propylene glycol alginate that serves as the principle, primary or sole film former of the coating composition. The coatings of the present invention can be applied to **pharmaceutical**, including neutraceutical, and veterinary solid dosage forms, such solid substrates such as seeds, animal feed, fertilizers, pesticide tablets and granules, . . . dispersed in aqueous media, and, when applied as a coating, provide high

L57 ANSWER 74 OF 79 USPAT2 on STN (Continued)
lustre coatings which do not retard or extend **release** of active ingredient from a coated substrate.
SUMM It is a common practice to coat **pharmaceutical** and veterinary tablets to obtain several advantages. Among these are to improve the surface characteristics of tablets to make them . . .
SUMM Another very important function of a **pharmaceutical** or veterinary tablet coating is to improve the integrity of the tablet itself. Uncoated tablets are often subject to being. . .
SUMM . . . proportion to the increase in disintegration time. Many other agents commonly used in coating compositions are also known to delay **release** of **pharmaceutical** agents, such as enteric coatings which use polymeric film forming materials which are insoluble in water, or gastric fluid, some of these being specifically selected to by-pass both the stomach and small intestine and provide colonic **release**.
SUMM The coatings of this invention meet U.S. **Pharmacopeia** standards for rapid or immediate dissolution (U.S.P. monograph 23) of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates. Thus, they do not adversely impact or retard **release** of active ingredients from a substrate coated with them. Further, the coatings of this invention are readily dispersed and rapidly. . . .
SUMM . . . a secondary film former and/or a strengthening polymer as an additional ingredient. More specifically, the present invention provides
a prompt **release**, edible, hardenable PGA coating composition, as well as dry coatings and aqueous dispersions thereof and solid dosage forms coated therewith.
DETD For purposes of this application, the term "edible" is intended to mean food or **pharmaceutical** grade materials which are approved by regulatory authorities for use in **pharmaceutical** or food applications. The term "hardenable," used to describe the coating compositions of this
invention, is intended to include only. . . this invention or tablets
coated with the compositions of this invention, mean that the coatings of this invention meet U.S. **Pharmacopeia** standards (U.S.P. monograph 23) for rapid or immediate dissolution of active ingredients from tablets or other solid dosage forms coated with them. Thus, they provide
prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates.
They do not, when placed in water or ingested, adversely impact or retard **release** or dissolution of tablets or other dosage forms coated with them. Coatings made in accordance with the present invention are. . .
DETD . . . glycol alginate provides important film-forming characteristics
required to provide an elegant coating which is particularly useful in, for example, coating **pharmaceutical** and veterinary tablets, caplets, granules, and spheres which contain active ingredients which require **release** promptly after being placed in aqueous media or ingested.

L57 ANSWER 74 OF 79 USPAT2 on STN (Continued)
.sp.2Hydroxylated soy lecithin, Central Soya
.sp.3Maltodextrin, Maltrin M180
.sp.4**Hydroxypropylcellulose** 250 L
.sp.5S = excellent; 4 = acceptable; 3 = marginal; 2 = poor; 1 = Not acceptable
.sp.6Not tested
CLM What is claimed is:
2. A solid dosage form coated with an edible, hardenable, prompt **release** coating composition comprising 55% to 85% of propylene glycol alginate and up to 10% of a surfactant, wherein the propylene. . .
CLM What is claimed is:
2. The solid dosage form of claim 1, wherein said solid dosage form is
a **pharmaceutical** or veterinary tablet.
CLM What is claimed is:
4. An edible, hardenable, prompt **release** coating composition comprising: at least one of a filler and a pigment, the filler being maltodextrin; and 55% to 85%
CLM What is claimed is:
6. An edible, hardenable, prompt **release** coating composition comprising: at least one of a filler and a pigment, the pigment forming from 5% to 25% of.
CLM What is claimed is:
8. An edible, hardenable, prompt **release** coating composition comprising 55% to 85% of propylene glycol alginate, 10% to 30% maltodextrin, and 2% to 10% lecithin, wherein
CLM What is claimed is:
10. The **coating** composition of claim 9 wherein **carrageenan** is present at 5% to 10% by dry weight of the composition.
CLM What is claimed is:
11. The coating composition of claim 9 where **hydroxyethylcellulose** is present at 5% to 10% by dry weight of the composition.
CLM What is claimed is:
12. An edible, hardenable, prompt **release** coating composition comprising 55% to 85% of propylene glycol alginate, 5% to 15% pigment, and 2% to 10% lecithin, wherein. . .

L57 ANSWER 74 OF 79 USPAT2 on STN (Continued)
DETD . . . may include a minor amount of secondary film former such as carrageenan or HPMC and/or a strengthening polymer such as **hydroxyethylcellulose**.
DETD . . . example, calcium carbonate, dicalcium phosphate and carbohydrates, such as starch, maltodextrin, lactose, mannitol and other
sugars, croscarmellose sodium, or microcrystalline **cellulose**. Of these, maltodextrin has been found beneficial at about 20% to about 30% by dry weight of the composition, but. . .
DETD . . . formulation, it may be desirable to include a secondary film former such as carrageenan and/or a strengthening polymer such as **hydroxyethylcellulose**. While these additional additives are generally not required, they may be utilized if desired at about 3% to about 12%. . . .
DETD . . . dry weight of the composition of a secondary film forming polymer such as carrageenan or a strengthening polymer such as **hydroxyethylcellulose**. Preservatives, such as methyl paraben at 0.75% by weight and/or propyl paraben at 0.075% to 0.15% may also be present. . . .
DETD . . . may be preferable to maintain agitation of the aqueous dispersion during the entire period of its being sprayed onto the **pharmaceutical** or veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizer, pesticide tablets, or food.
DETD The preferred edible, hardenable, prompt **release** coating formulations of this invention may generally be prepared and used according to a simple procedure. Propylene glycol alginate and. . .
DETD . . . thixotropic behavior of a formulation which sets up during overnight storage. Unlike coating formulations based primarily on hydroxyalkyl ethers of **cellulose**, for example, HPMC, constant stirring of the propylene glycol alginate-based formulations of this invention does not need to be continued.
DETD The level of coating applied to **pharmaceutical** or veterinary dosage forms is preferably between about 0.5% to about 4% by weight of the uncoated dosage form, more. . .
DETD All components of the formulation are typically **pharmaceutically** acceptable, edible food grade materials.
DETD . . . twin shell blender were placed 292 grams of low viscosity propylene glycol alginate (Protan Ltd., Manitoba, CA, Province/FMC Corporation) and 45 grams of **hydroxyethylcellulose** 250L, 22.5 grams of hydroxylated soy lecithin (Precept 8103, Central Soya), 45 grams of maltodextrin M 50 (Maltrin M1 50),. . .

	5	6	7	8			
Maltodextrin.sup.3	---	10	18	30		30	25
Pigment	13.4	10	10	--		7.5	10
HEC.sup.4	--	**10**	--	--		--	--
Iota **carrageenan**	--	--	--	--		--	5
Caplet Ingredients							
Acetaminophen						X	X
Ibuprofen	X	X	X				
Chlorpheniramine				X			
Coating Weight	3.	.	92		91		
60 minutes			99		97		

.sup.1Polypropylene glycol alginate (Profoam ®, Pronova/FMC Corporation)

L57 ANSWER 75 OF 79 USPAT2 on STN
ACCESSION NUMBER: 2002:203867 USPAT2
TITLE: Edible PGA coating composition
INVENTOR(S): Angelica, Michael, Marlboro, NJ, United States
Bliefernich, Eric, Yardville, NJ, United States
PATENT ASSIGNEE(S): FMC Corporation, Philadelphia, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6699315	B2	20040302
APPLICATION INFO.:	US 2001-994252		20011126 (9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-247778P	20010419 (60)	<--
	US 2001-268068P	20010214 (60)	<--
	US 2000-253406P	20001128 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Brunsman, David
LEGAL REPRESENTATIVE: Woodcock Washburn LLP
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 666
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An edible, hardenable coating composition is disclosed which comprises high levels of low viscosity propylene glycol alginate and a surfactant,
which may additionally contain a filler, a pigment, and optionally a small amount of a secondary film former and/or a strengthening polymer. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB . . . of a secondary film former and/or a strengthening polymer. The coating composition of the present invention may be applied to **pharmaceutical** and veterinary solid dosage forms, confectionery, seeds, animal feed, fertilizers, pesticide tablets, and foods and provides an elegant prompt **release** coating which does not retard the **release** of active ingredients from the coated substrate.
SUMM This invention relates to edible, hardenable prompt **release** coating compositions comprising a film forming amount of low viscosity propylene
glycol alginate that serves as the principle, primary or sole film former of the coating composition. The coatings of the present invention
can be applied to **pharmaceutical**, including neutraceutical, and veterinary solid dosage forms, such solid substrates as seeds, animal feed, fertilizer, pesticide tablets and granules, dispersed in aqueous media, and, when applied as a coating, provide high
lustre coatings which do not retard or extend **release** of active ingredient from a coated substrate.

L57 ANSWER 75 OF 79 USPAT2 on STN (Continued)

SUMM It is a common practice to coat **pharmaceutical** and veterinary tablets to obtain several advantages. Among these are to improve the surface characteristics of tablets to make them . . .

SUMM Another very important function of a **pharmaceutical** or veterinary tablet coating is to improve the integrity of the tablet itself. Uncoated tablets are often subject to being . . .

SUMM . . . proportion to the increase in disintegration time. Many other agents commonly used in coating compositions are also known to delay **release** of **pharmaceutical** agents, such as enteric coatings which use polymeric film forming materials which are insoluble in ether, or gastric fluid, some of these being specifically selected to by-pass both the stomach and small intestine and provide colonic **release**.

SUMM The coatings of this invention meet U.S. **Pharmacopoeia** standards for rapid or immediate dissolution (U.S.P., monograph 23) of active ingredients from tablets or other solid dosage forms coated with them. They provide prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrates. Thus, they do not adversely impact or retard **release** of active ingredients from a substrate coated with them. Further, the coatings of this invention are readily dispersed and rapidly. . .

SUMM . . . a secondary film former and/or a strengthening polymer as an additional ingredient. More specifically, the present invention provides

a prompt **release**, edible, hardenable PGA coating composition, as well as dry coatings and aqueous dispersions thereof and solid dosage forms coated therewith.

SUMM For purposes of this application, the term "edible" is intended to mean food or **pharmaceutical** grade materials which are approved by regulatory authorities for use in **pharmaceutical** or food applications. The term "hardenable," used to describe the coating compositions of this

invention, is intended to include only. . . this invention or tablets

coated with the compositions of this invention, mean that the coatings of this invention meet U.S. **Pharmacopoeia** standards (U.S.P. monograph 23) for rapid or immediate dissolution of active ingredients from tablets or other solid dosage forms coated with them. Thus, they provide

prompt **release** or dissolution consistent with the **release** rates which is normally obtained with the uncoated tablets or other substrate.

They do not, when placed in water or simulated, adversely impact or retard **release** or dissolution of tablets or other dosage forms coated with them. Coatings made in accordance with the present invention are. . .

SUMM . . . glycol alginate, provides important film-forming characteristics required to provide an elegant coating which is particularly useful in, for example, coating **pharmaceutical** and veterinary tablets, caplets, granules, and spheres which contain active ingredients which require **release** promptly after being placed in aqueous media or ingested.

SUMM . . . may include a minor amount of secondary film former such as carrageenan or HPMC and/or a strengthening polymer such as

L57 ANSWER 75 OF 79 USPAT2 on STN (Continued)

.sup.1Polypropylene glycol alginate (Profoam **®**, Pronova/FMC Corporation)

.sup.2Hydroxylated soy lecithin, Central Soya

.sup.3Maltodextrin, Maltrin M180

.sup.4**Hydroxypthylcellulose** 230.

.sup.5T = excellent; 4 = acceptable; 3 = marginal; 2 = poor; 1 = Not acceptable

.sup.6Not tested

CLM What is claimed is:

1. An edible, hardenable, prompt **release** coating composition comprising 5% to 90% of propylene glycol alginate and 2% to 10% of a surfactant, wherein the propylene . . .

CLM What is claimed is:

10. The **coating** composition of claim 9 wherein **carrageenan** is present at 5% to 10% by dry weight of the composition.

CLM What is claimed is:

11. The coating composition of claim 9 where **hydroxythylcellulose** is present at 5% to 10% by dry weight of the composition.

L57 ANSWER 76 OF 79 USPAT2 on STN (Continued)

hydroxypthylcellulose. . .

SUMM . . . example, calcium carbonate, dicalcium phosphate and carbohydrates, such as starch, maltodextrin, lactose, mannitol and other

sugars, croscarmelose sodium, or microcrystalline **cellulose**. Of these, maltodextrin has been found beneficial at about 10% to about 30% by dry weight of the composition, but. . .

SUMM . . . formulation, it may be desirable to include a secondary film former such as carrageenan and/or a strengthening polymer such as **hydroxypthylcellulose**. While such additional additives are generally not required, they may be utilized if desired at about 3% to about 12%

by dry weight of the composition of a secondary film forming polymer such as carrageenan or a strengthening polymer such as **hydroxypthylcellulose**. Preservatives, such as methyl paraben at 0.75% to 1.50% and/or propyl paraben at 0.075% to 0.15% may also be present. . . .

SUMM . . . may be preferable to maintain agitation of the aqueous dispersion during the entire period of its being sprayed onto the **pharmaceutical** or veterinary solid dosage form, confectionery, seeds, animal feed, fertilizer, pesticide tablets, or food.

SUMM The preferred edible, hardenable, propyl **release** coating formulations of this invention may generally be prepared and used according to a simple procedure. Propylene glycol alginate and. . .

SUMM . . . thixotropic behavior of a formulation which sets up during overnight storage. Unlike coating formulations based primarily on hydroxyalkyl ethers of **cellulose**, for example, HPMC, constant stirring of the propylene glycol alginate-based formulations of this invention does not need to be continued.

SUMM The level of coating applied to **pharmaceutical** or veterinary dosage forms is preferably between about 0.5% to about 4% by weight of the uncoated dosage form, more. . .

SUMM All components of the formulation are typically **pharmaceutically** acceptable, edible food grade materials.

DETD . . . twin shell blender were placed 282 grams of low viscosity propylene glycol alginate (Profoam, Pronova/FMC Corporation) and 47 grams of **hydroxythylcellulose** 250L, 22.5 grams of hydroxylated soy lecithin (Precept 8105, Central Soya), 45 grams of maltodextrin M1 90 (Maltrin M1 90,. . .

DETD . . . 55

Lecithin.sup.2 3.3 5 7 5 2.5 5

Maltodextrin.sup.3 -- 10 18 30 30 25

Pigment 13.4 10 10 -- 7.5 10

HEC.sup.4 -- **10** -- -- -- --

Iota **carrageenan** -- -- -- -- -- 5

Caplet Ingredients

Acetaminophen X X

Ibuprofen X X X

Chlorpheniramine X

Coating weight 3 3 3 3 3 3

(%)

Friability . . minutes 92 91

60 minutes 99 99

L57 ANSWER 76 OF 79 USPAT2 on STN

ACCESSION NUMBER: 2002:157579 USPAT2

TITLE: Low-density compositions and particulates including same

INVENTOR(S): Christensen, Jr., Robert I., Paule, CA, United States
Genencor International, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6534466	B2	20030318
APPLICATION INFO.:	US 2000-479693		20000107 (9) <--

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115255P	19990108 (60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Gupta, Yogendra N.
ASSISTANT EXAMINER: Elhilo, Eisa
LEGAL REPRESENTATIVE: Genencor International, Inc.
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 9464
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides low-density compositions, as well as particulates formed, at least in part, from such compositions.

Preferred low-density materials include, for example, hollowspheres, low-density minerals, and low-density wood materials (e.g., sawdust). The low-density compositions of the invention can be formed as particulates, or cores, suitable for use in forming enzyme granules, e.g., marums, layered granules, prills, drun granules, agglomerated granules, or the like. Granules are disclosed having advantageous properties, e.g., low dusting, storage stable, fast enzyme-**release** profile, low true density, etc. The granules of the invention are especially useful, for example, in liquid detergents and cleaners, e.g., predominantly aqueous, liquid laundry detergents. In one embodiment, granules are provided having a true, or volumetric, density within a range of from about 0.95 to about 1.4 g/cm.sup.3. The granules can be economically produced in commercial quantities by way of a marumerization, drun granulation, fluid-bed spray-coating, pan-coating, or other suitable process.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . prills, drun granules, agglomerated granular, or the like. Granules are disclosed having advantageous properties, e.g., low dusting, storage stable, fast enzyme-**release** profile, low true density, etc. The granules of the invention are especially useful, for example, in liquid detergents and cleaners.

SUMM The use of proteins such as **pharmaceutically** important protein, e.g., hormones, and industrially important proteins, e.g., enzymes, has been rapidly growing in recent years. Today, for example, . . .

SUMM U.S. Pat. No. 4,106,991 describes an improved formulation of enzyme granules by including within the composition undergoing granulation,

L57 ANSWER 76 OF 79 USPAT2 on STN (Continued)
finely divided **cellulose** fibers in an amount of 2-40% w/w based on the dry weight of the whole composition. In addition, this patent. . . .
. . . diatomaceous earth or sodium citrate crystals. The film forming
material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.
SUM . . . of providing sufficient enzyme activity in the wash. It is also
generally desirable to have granule with a relatively fast **release** profile. Thus, the enzyme load for such granule needs to be protected from the various harsh components of the liquid. . . . sodium perborate
or sodium percarbonate, and the like), yet the means of achieving such protection must not unduly hinder enzyme **release** as it is known by those working in the field, it is often problematic to simultaneously provide good protection for the enzyme and a fast **release** profile. . . . environment so that they remain active throughout the product
. . . lifecycle. It is also desirable to have a relatively fast enzyme **release** profile.
SUM . . . a true density less than 1.4 g/cm.sup.3; they exhibit sufficient enzyme activity in the wash; they have a relatively fast enzyme **release** profile; they have relatively low susceptibility to attrition& breakdown; they tend to remain dispersed and suspended in the liquid detergent.
SUM . . . in storage (e.g., greater than 50%). Moreover, an especially desirable granule would exhibit relatively slow release quickly in the wash liquor to **release** its enzyme activity. It is an advantage of the present invention to provide granules meeting such specifications.
SUM . . . dent starch, modified starches (e.g., hydroxypropyl addition, ethoxylation, acetylation, and thinning of), sugars (e.g., sucrose, dextrose, fructose, lactose etc.), maltodextrin, **polyvinylpyrrolidone** (PVP), polyethylene glycol (PEG), xanthum gum, gum arabic, acacia gum, alginate, carrageenan, waxes (e.g., carnuba, beeswax, paraffin and blends
thereof),.
SUM Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as enzymes.
SUM Suitable coatings include water soluble or water dispersible film-forming polymers such as **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose** (MC), hydroxypropyl **methylcellulose** (HPMC), hydroxyethyl **cellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, gum arabic, xanthan, **carrageenan**, chitosan, latex polymers, and enteric **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.
SUM . . . Preferably, the outer coating layer comprises partially hydrolysed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVA/methylmethacrylate copolymer and PVP-PVA copolymer and enteric co-polymers such as those sold under the . . .

L57 ANSWER 77 OF 79 USPAT2 on STN
ACCESSION NUMBER: 2002:157138 USPAT2
TITLE: Coated particles containing an active
INVENTOR(S): Swinkels, Ola, Soborg, DENMARK
Bach, Poul, Birkerod, DENMARK
Novozymes A/S, Bagsvaerd, DENMARK (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 7070820	B2	20060704
APPLICATION INFO.:	US 2001-948949	20010928	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	DK 2000-1460	20000922
	US 2000-235005P	20000906 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Reddick, Keith
LEGAL REPRESENTATIVE: Lambiris, Elias J.
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 2247
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB . . . The present invention relates to coated particles comprising a coating and a core particle comprising an active, wherein the coating comprises a gas phase component. The invention also relates to processes for the manufacture of such coated particles comprising (a) providing a coating material comprising a gas phase component and applying the gas containing coating material to a core particle or (b) providing a coating material comprising a gas phase component, spraying the coating material to a core particle and treating the coated particles so
as to generate a gas from the gas generating component. Furthermore, it also relates to the use of such coated particles in a number of applications.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM . . . various high-shear mixers can be used as granulators, granulates consisting of the enzyme, fillers and binders etc. are mixed with **cellulose** fibers to reinforce the particles to give the so-called T-granulate. Reinforced particles, being more robust, release less enzymatic dust (wide-
SUM . . . Also polysaccharides are preferred, such as starch or derivatives thereof. Roda.sup.R is an example of non-hollow lightweight material made from **cellulose** (waste from papermaking), available from GranTek Inc. These materials may be included in the granules of the invention either alone.
SUM . . . Further embodiments waxes which are useful in the invention can
be found in C. M. McTaggart et. al., Int. J. **Pharm.** 19, 179 (1984) or Flanders et al., Drug Dev. Ind. **Pharm.** 13, 1001 (1987) both incorporated herein by reference.
SUM Carbohydrate polymers may be selected from pectin, starch, modified starch, **cellulose**, modified **cellulose**, carrageenan, gum Arabic, acacia gum, xanthan gum, locust bean gum and guar gum. As employed in

L57 ANSWER 76 OF 79 USPAT2 on STN (Continued)
DETD . . . desired-60 fluid bed coater and fluidized. To that, 65.5 Kgs of
a solution containing 7.7% active alkalase protease and 2.1% **polyvanylpyrolidone** (Luviskol K-17 from BASF) was spray-coated onto the cores. Subsequently, a 40% solids solution containing 4.8 Kg of dry corn. . . . Kgs of hydrated starch was spray-coated onto the enzyme particulates. Finally, a cosmetic coating solution containing 3.42 Kgs of hydroxymethyl **cellulose** (Methocel E from Dow chemical), 6.252 Kgs of titanium dioxide and 0.733 Kgs of polyethylene glycol (PEG 600) was spray-coated.
DETD c) 600 grams of **cellulose** fibers (Arbocel 600-70)
DETD g) 79 grams of **polyvinylpyrolidone** (Luviskol K-90 from BASF)
DETD . . . of 85.degree. fluidizing air. To this, 1710 grams of a 17% w/w total solids solution containing 7% active alkalase protease and 168% grams of a liquid enzyme concentrate containing 7.4% alkaline protease was spray-coated onto the low density of . . . coated onto the enzyme matrum. Subsequently, 1520 grams of a 13% w/w total solids solution including 30 grams of hydroxypropyl **methylcellulose** (Methocel E-15), 99 grams of titanium dioxide and 17 grams of polyethylene glycol (PEG900) was sprayed coated onto the harder as. . .
DETD c) 600 grams of **cellulose** fibers (Arbocel 600-70)
DETD g) 79 grams of **polyvinylpyrolidone** (Luviskol K-90 from BASF)
DETD . . . coated onto the enzyme matrum. Subsequently, 1520 grams of a 13%
w/w total solids solution including 74 grams of hydroxypropylmethyl **cellulose** (Methocel E-15), 99 grams of titanium dioxide, 70 grams of neodol 23/6.5 (Shell chemical) and 15 grams of polyethylene glycol. .
DETD . . . was spray-coated onto the sucrose seeds. Subsequently, 56.3 Kgs
of a 17% w/w total solids solution containing 3.3 Kgs hydroxypropylmethyl **cellulose** (Methocel E-15), 3.3 Kgs titanium dioxide and 0.7 Kgs of polyethylene glycol (PEG 600) was spray coated onto the enzyme.
DETD Enzyme **Release**
DETD A commonly used method for measuring enzyme **release** from a granule under typical liquid applications conditions is the enzyme dissolution test. In this test, granules are added to. . .
DETD Granules of the present invention preferably have at least 90%, and preferably at least 95%, of the enzyme activity **released** into the liquor within 5 minutes at 15.degree. C. More preferably, the granules taught herein have a minimum of 90% of the enzyme activity **released** into the liquor within 3 minutes at 15.degree. C. Exemplary granules that have been tested in support of the present invention exhibit an enzyme **release** rate of no less than 90% in 5 minutes at 15.degree. C, and most exhibit an enzyme **release** rate of no less than 90% in 3 minutes at 15.degree. C.

L57 ANSWER 77 OF 79 USPAT2 on STN (Continued)
the context of the.
SUM . . . (see, e.g. A. Xu and P. A. Seib, Cereal Chem. 70 (1993), pp. 463-470). Synthetic polymers may be selected from **polyvinyl** pyrrolidone (PVP), **polyvinyl** alcohol (PVA), **polyvinyl** acetate, polyethylene, polymethacrylate, polyacrylamide, polysulfonate, polyacrylonitrile, and copolymers thereof, in particular water soluble polymers or copolymers.
SUM . . . described in WO 96/41859 both disclosures incorporated herein by reference. Still other examples of useful enzyme stabilizers are gelatine, casein, **Polyvinyl** pyrrolidone (PVP) and powder of skimmed milk. The amounts of protective agent in the coating may be 5-40% w/w of. . . methods, serve to increase the solubility of formulations, and typical agents known to the art include, for example, **Pharmacopeia's**. Thus, the core particle may optionally comprises any agent that serves to enhance the solubility of the granule. Such agents include, for example, acids and/or silicates.
Binders, e.g. binders with a high melting point or indeterminately high melting
points and of a non-waxy nature, e.g. **polyvinyl** pyrrolidone, dextrins, **polyvinylalcohol**, **cellulose** derivatives, for example hydroxypropyl **cellulose**, methyl **cellulose** or CMC. A suitable binder is a carbohydrate binder such as Glucidex 21D.TM. available from Roquette Freres, France.
Fiber materials such as pure or impure **cellulose** in fibrous form. This can be sawdust, pure fibrous **cellulose**, cotton, or other forms of pure or impure fibrous **cellulose**. Also, filter aids based on fibrous **cellulose** can be used. Examples of **cellulose** and fibrous fors are on the market, e.g. CEFO.TM. and ARBOCELL.TM.. Pertinent examples of
fibrous **cellulose** filter aids are is Arbocel BFC200.TM. and Arbocel BC200.TM. Also synthetic fibers may be used as described in EP 304331 B1 and typical fibers may be made of polyethylene, polypropylene, polyester, especially nylon, **polyvinyl**-formats, poly(meth)acrylic compounds.
Cross-linking agents such as enzyme-compatible surfactants, e.g. ethoxylated alcohols, especially ones with 10 to 80 ethoxy groups. These may. . .
SUM . . . content, the term "carbohydrate" is used to denote not only enzymes capable of breaking down carbohydrate chains (e.g. starches or **cellulose**) of especially five- and six-membered ring structures (i.e. glycosidases, EC 3.2), but also enzymes capable of isomerizing carbohydrates, e.g. six-membered. . . .
SUM . . . the use of the composition, e.g. for improving foodstuffs such as bread or for cleaning an object such as a **cellulose** containing fabric.
SUM The detergent may comprise one or more polymers. Examples are **carboxymethylcellulose**, poly(vinylpyrrolidone), poly(1-vinylpyrrolyl), poly(vinyl alcohol), poly(vinylpyridine-N-oxide), poly(vinylimidazole), polycarboxylates such as polyacrylates, maleic/acrylic acid copolymers and lauryl methacrylate/acrylic acid copolymers.
DETD The production of foam according to the invention was tested using a coating feed consisting of:

12.5 kg **polyvinyl** alcohol (PVA) (Mowiol 4-88 obtainable from Hoechst, Germany) as polymer
6.25 kg glycerol (99.5%) as plastisizer
32.25 kg H.sub.2O (demineralised) as solvent
CLM What is claimed is:
. . . The particle of claim 8, wherein the carbohydrate polymer is selected

L57 ANSWER 77 OF 79 USPAT2 on STN (Continued)
from the group consisting of pectin, starch, modified starch, **cellulose**, modified **cellulose**, carrageenan, gum Arabic, acacia gum, xanthan gum, locust bean gum and guar gum.

IT 71-52-3, Bicarbonate, uses 79-10-7P, Acrylic acid, esters, polymers 79-41-4D, Methacrylic acids, esters, polymers 124-38-9, Carbon dioxide, uses 7727-37-9, Nitrogen, uses 9000-01-5, Gum arabic **9000-07-1**, Carrageenan 9012-76-4, Cellulose acetate 9000-20-7, Guar gum 9000-40-2, Locust bean gum 9000-69-5, Pectin 9002-90-2, Formamyl 9002-89-5, Poly(vinyl alcohol) 9003-05-8, Polyacrylamide 9003-39-8, Poly(vinyl acetate) 9003-39-8, PVP 9004-34-6, **Cellulose**, uses 9005-25-8, Starch, uses 9012-76-4, Chitosan 11138-66-2, Xanthan gum 24991-23-9 25322-68-3, Polyethylene glycol 25513-46-6, Poly(glutamic acid) 25608-40-6, Poly(aspartic acid) 26062-11-8, Poly(aspartic acid) 136040-76-5, Expancel 461DE20
(coated particles containing active substance for detergent formulations)

IT **9000-07-1**, Carrageenan
(coated particles containing active substance for detergent formulations)

L57 ANSWER 78 OF 79 USPAT2 on STN
ACCESSION NUMBER: 2002:13860 USPAT2
TITLE: Granule containing protein and salt layered on an inert particle
INVENTOR(S): Becker, Nathaniel Y., Burlingame, CA, United States
Christensen, Jr., Robert L., Finole, CA, United States
Gros, Ernst E., Kantvik, FINLAND
PATENT ASSIGNEE(S): Genencor International, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6423511	B2	20020723
APPLICATION INFO.:	US 1998-215984		19981218 (9) <--
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1997-995430, filed on 29 Dec 1997, now abandoned		

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Naff, David M.
LEGAL REPRESENTATIVE: Genencor International, Inc.
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 557
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Granules are prepared containing an admixture of protein and salt layered over an inert particle. A preferred amount of salt is about between 63.7 and 84.3% of the total weight of the admixture. Proteins include **pharmaceutically** important proteins such as hormones, or industrially important proteins such as enzymes including proteases, amylases, lipases and cellulases capable of hydrolyzing substrates such as stains. Inert particles include inorganic salts, sugars, sugar alcohols, small organic molecules such as organic acids or salts, and minerals such as clays or silicates. A binder such as starch or polyethylene oxide may be mixed in with the admixture. A barrier material such as an inorganic salt or organic acid or salt may be in the
admixture or coated over the admixture layer. A coating layer of a soluble or water dispersible film-forming polymer may be between the inert particle and admixture layer and/or over the admixture layer. The granules may also contain plasticizers, extenders, lubricants, pigments and anti-agglomeration agents. A preferred method for preparing the granules is by spraying a solution or slurry of the admixture onto the inert particles while fluidized in a fluid-bed coater.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . A preferred amount of salt is about between 63.7 and 84.3% of the total weight of the admixture. Proteins include **pharmaceutically** important proteins such as hormones, or industrially important proteins such as enzymes including proteases, amylases, lipases and cellulases capable of

SUMM Proteins such as **pharmaceutically** important proteins like hormones and industrially important proteins like enzymes are becoming more widely

L57 ANSWER 78 OF 79 USPAT2 on STN (Continued)
used. Enzymes, for example, are used. . . .

SUMM U.S. Pat. No. 4,106,991 describes an improved formulation of enzyme granules by including within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-40% w/w based on the dry weight of the whole composition. In addition, this patent. . . .

SUMM . . . diatomaceous earth or sodium citrate crystals. The film forming
material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.

SUMM . . . and improved stability formulations. Accomplishing all these desired characteristics simultaneously is a particularly challenging task since, for example, many delayed **release** or low-dust agents such as fibrous **cellulose** or wax wire size polymers leave behind insoluble residues.

SUMM . . . There can be one or more layers between the seed particle and the matrix, for example, a coating such as **polyvinyl** alcohol.

SUMM Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as enzymes.

SUMM . . . natural polymers such as starch, modified starch, carrageenan, gum arabic and guar gum and synthetic polymers such as polyethylene oxide, **polyvinyl** pyrrolidone, polyethylene glycol and polyethylene oxide/propylene oxide.

SUMM Suitable coatings include water soluble or water dispersible film-forming polymers such as **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose, hydroxycellulose, ethylcellulose,** carboxymethyl **cellulose,** hydroxypropyl **cellulose,** polyethylene glycol, polyethylene oxide, gum arabic, xanthan, **carrageenan,** chitosan, latex polymers, and enteric **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.

SUMM . . . Preferably, the outer coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVA-methylmethacrylate copolymer and PVP-PVA copolymer.

DETD . . . cosmetically coated with 2116 grams of an aqueous solution containing 131 grams (6.2% w/w) titanium dioxide, 53 grams (2.5% w/w) **methylcellulose** named under the trade name Methocel A-15LV (Dow Chemical Comp.), 53 grams (2.5% w/w) of maltodextrin M150 (DE=15 from Grain.

CLM What is claimed is:
. . . wherein the binder is selected from the group consisting of starch, modified starch, carrageenan, gum arabic, guar gum, polyethylene oxide, **polyvinyl** pyrrolidone, and polyethylene glycol.

CLM What is claimed is:
8. The granule of claim 6, wherein the coating is selected from the group consisting of **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose, hydroxycellulose, ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan and carrageenan.

CLM What is claimed is:
. . . wherein the binder is selected from the group consisting of starch,

L57 ANSWER 78 OF 79 USPAT2 on STN (Continued)
modified starch, carrageenan, gum arabic, guar gum, polyethylene oxide, **polyvinyl** pyrrolidone, and polyethylene glycol.

CLM What is claimed is:
24. The method of claim 22, wherein the coating is selected from the group consisting of **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose, hydroxycellulose, ethylcellulose**, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan and carrageenan.

L57 ANSWER 79 OF 79 USPAT2 on STN
ACCESSION NUMBER: 2007:192559 USPAT2
TITLE: Fluidized bed low density granule
INVENTOR(S): Dale, Douglas A., Pacifica, CA, United States
Genencor International, Inc., Palo Alto, CA, United States (U.S. corporation)
PATENT ASSIGNEE(S):

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6835611	B2	20041221
APPLICATION INFO.:	US 2001-964210		20010925 (9) <--
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-462431, filed on 7 Jan 2000, now patented, Pat. No. US 6319827		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-109417P	19981117 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Borgeest, Lorna M.	
LEGAL REPRESENTATIVE:	Genencor International, Inc.	
NUMBER OF CLAIMS:	19	
EXEMPLARY CLAIM:	1,15	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	733	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Low-density enzyme-carrying granules are low dusting and/or storage-stable, and especially suitable for use in liquid detergents and cleaners, such as non-aqueous liquid laundry detergents. Preferred granules of the invention include a relatively high content of one or more low-density fillers, such as perlite or starch, to provide a desired product density. In one embodiment, the granules have a true density within a range of from about 1 to about 1.4 g/cm.sup.3. The granules can be economically produced in commercial quantities using fluidized bed technology.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUM1 The use of proteins such as **pharmaceutically** important proteins, e.g., hormones, and industrially important proteins, e.g., enzymes, has been rapidly growing in recent years. Today, for example, . . .

SUM2 U.S. Pat. No. 4,106,991 describes an improved formulation of enzyme granules by including within the composition undergoing granulation, finely divided **cellulose** fibers in an amount of 2-40% w/w based on the dry weight of the whole composition. In addition, this patent. . . . forming . . . diatomaceous earth or sodium citrate crystals. The film material may be a fatty acid ester, an alkoxylated alcohol, a **polyvinyl** alcohol or an ethoxylated alkylphenol.

SUM3 . . . . in storage (e.g., greater than 50%). Moreover, an especially desirable granule would additionally disintegrate quickly in the wash liquor to **release** its enzyme activity. It is an advantage of the present invention to provide granules meeting such specifications.

SUM4 . . . porous material. For example, the filler can be selected from one or more of the following: perlite, fumed silica, starch, **cellulose** fibers, DE, feather particles, zeolites, flour, fragments of milled plant-derived materials.

SUM5 Acceptable fillers include perlite, fumed silica, starch, **cellulose** fibers, DE, feather particles, zeolites, flour, fragments of milled plant-derived materials, and any mixture thereof. Particularly preferred fillers are porous.

SUM6 Acceptable fillers include starch, **cellulose** fibers, DE, feather particles, zeolites (such as used for molecular sieving), flour, milled plant derived fragments such as corn cobs, . . .

SUM7 Proteins that are within the scope of the present invention include **pharmaceutically** important proteins such as hormones or other therapeutic proteins and industrially important proteins such as enzymes.

SUM8 Suitable synthetic polymers include polyethylene oxide, **polyvinyl** alcohol, **polyvinyl** pyrrolidone, **polyvinyl** pyridine, polyethylene glycol and polyethylene oxide/polypropylene oxide.

SUM9 Suitable coatings include water soluble or water dispersible film-forming polymers such as **polyvinyl** alcohol (PVA), **polyvinyl** pyrrolidone (PVP), **cellulose** derivatives such as **methylcellulose**, hydroxypropyl **methylcellulose**, **hydroxycellulose**, **ethylcellulose**, carboxymethyl **cellulose**, hydroxypropyl **cellulose**, polyethylene glycol, polyethylene oxide, gum arabic, xanthan, **carrageenan**, chitosan, latex polymers, and enteric **coatings**. Furthermore, coating agents may be used in conjunction with other active agents of the same or different categories.

SUM10 . . . Preferably, the outer coating layer comprises partially hydrolyzed PVA having low viscosity. Other vinyl polymers which may be useful include **polyvinyl** acetate and **polyvinyl** pyrrolidone. Useful copolymers include, for example, PVA-methylmethacrylate copolymer and PVP-PVA copolymer and enteric co-polymers such as those sold under the . . .

DET2 . . . applied using 50 psi atomization pressure. To the resulting product, a solution of 117 g titanium dioxide, 94 g methyl **cellulose** (Methocel A15), 32 g polyethylene glycol (PEG 600) and 19 g surfactant (Neodol 23-6.5) was applied. The resulting product weighed. . . .

DET3 . . . applied using 50 psi atomization pressure. To the resulting product, a solution of 117 g titanium dioxide, 94 g methyl **cellulose** (Methocel A15), 32 g polyethylene glycol (PEG 600) and 19 g surfactant (Neodol 23-6.5) was applied. The resulting product weighed. . . .

DET4 . . . g water was applied using 50 psi. To the resulting product, a solution of 128 g titanium dioxide, 102 g **polyvinyl** alcohol (Vinanol 51-05) and 26 g surfactant (Neodol 23-6.5) in 904 g water was applied. The resulting product weighed 1609.

DET5 . . . air and 100 C. inlet air temperature. To the resulting product, a solution of 9.75 kg titanium dioxide, 7.8 kg **polyvinyl** alcohol (Elvanol 51-05) and 1.95 kg surfactant (Neodol 23-6.5) in 69.14 kg water was applied. The resulting product weighed 169.0.

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     (FILE 'HOME' ENTERED AT 12:33:20 ON 18 MAR 2010)

     FILE 'USPATFULL, USPATOLD, USPAT2' ENTERED AT 12:33:34 ON 18 MAR 2010
L1        24050 SEA SPE=ON  ABB=ON  PLU=ON  CARRAGEENAN
L2           60 SEA SPE=ON  ABB=ON  PLU=ON  L1 (3A) SHELL?
L3           12 SEA SPE=ON  ABB=ON  PLU=ON  L2 AND PD<20010928
L4            9 SEA SPE=ON  ABB=ON  PLU=ON  L2 AND PRD<20010928
L5           12 SEA SPE=ON  ABB=ON  PLU=ON  L2 AND PD<20010928
L6        20334 SEA SPE=ON  ABB=ON  PLU=ON  L1 AND ?CELLULOS?
L7        13401 SEA SPE=ON  ABB=ON  PLU=ON  L1 AND ?POLYVINYL?

     FILE 'REGISTRY' ENTERED AT 12:35:31 ON 18 MAR 2010
L8          235 SEA SPE=ON  ABB=ON  PLU=ON  ?CARRAGEENAN?/CNS

     FILE 'USPATFULL, USPATOLD, USPAT2' ENTERED AT 12:35:45 ON 18 MAR 2010
L9         3953 SEA SPE=ON  ABB=ON  PLU=ON  L8
L10       24819 SEA SPE=ON  ABB=ON  PLU=ON  L1 OR L9
L11       20768 SEA SPE=ON  ABB=ON  PLU=ON  L10 AND (L6 OR L7)
L12         253 SEA SPE=ON  ABB=ON  PLU=ON  L1 (5A) (SHELL? OR COAT?)
L13         236 SEA SPE=ON  ABB=ON  PLU=ON  L12 AND (?CELLULOS? OR ?POLYVINYL?)

L14          74 SEA SPE=ON  ABB=ON  PLU=ON  L13 AND PRD<20010928
L15          67 SEA SPE=ON  ABB=ON  PLU=ON  L13 AND PD<20010928
L16          92 SEA SPE=ON  ABB=ON  PLU=ON  L13 AND AD<20010928
L17         127 SEA SPE=ON  ABB=ON  PLU=ON  (L14 OR L15 OR L16)
L18          72 SEA SPE=ON  ABB=ON  PLU=ON  L17 AND PHARM?/BI
                D KWIC 1-5
L19          59 SEA SPE=ON  ABB=ON  PLU=ON  L18 AND RELEAS?
L20           3 SEA SPE=ON  ABB=ON  PLU=ON  L19 AND GELLAN GUM?
                D KWIC 1-3
                D BIB 3
                D BIB 1-2
L21        4508 SEA SPE=ON  ABB=ON  PLU=ON  L1 (5A) 1##
                D KWIC 1-3
L22        3862 SEA SPE=ON  ABB=ON  PLU=ON  L1 (3A) 1##
L23        2398 SEA SPE=ON  ABB=ON  PLU=ON  L1 (3A) 2##
L24          25 SEA SPE=ON  ABB=ON  PLU=ON  (L22 OR L23) AND L19
                D KWIC 1-25
                D BIB 24-25
L25         305 SEA SPE=ON  ABB=ON  PLU=ON  L8 (L) (SHELL? OR COAT?)/IT
                D KWIC 1-3
                D KWIC 1-5
L26          76 SEA SPE=ON  ABB=ON  PLU=ON  L8 (2W) (SHELL? OR COAT?)/IT
                D KWIC 1-4
L27          14 SEA SPE=ON  ABB=ON  PLU=ON  L26 AND GELLAN GUM?/BI,IT
L28           3 SEA SPE=ON  ABB=ON  PLU=ON  L27 AND PRD<20010928
L29           3 SEA SPE=ON  ABB=ON  PLU=ON  L27 AND PD<20010928
L30           3 SEA SPE=ON  ABB=ON  PLU=ON  L27 AND AD<20010928
L31           5 SEA SPE=ON  ABB=ON  PLU=ON  (L28 OR L29 OR L30)
                D KWIC 1-5
L32           3 SEA SPE=ON  ABB=ON  PLU=ON  L31 AND PHARM?
L33         130 SEA SPE=ON  ABB=ON  PLU=ON  L26 OR L19
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L34          24 SEA SPE=ON  ABB=ON  PLU=ON  L26 AND PRD<20010928
L35          23 SEA SPE=ON  ABB=ON  PLU=ON  L26 AND PD<20010928
L36          25 SEA SPE=ON  ABB=ON  PLU=ON  L26 AND AD<20010928
L37          27 SEA SPE=ON  ABB=ON  PLU=ON  L26 AND AD<20010929
L38          23 SEA SPE=ON  ABB=ON  PLU=ON  L26 AND PD<20010929
L39          24 SEA SPE=ON  ABB=ON  PLU=ON  L26 AND PRD<20010929
L40          37 SEA SPE=ON  ABB=ON  PLU=ON  (L37 OR L38 OR L39)
L41          17 SEA SPE=ON  ABB=ON  PLU=ON  L40 AND PHARM?/BI,IT
L42          17 SEA SPE=ON  ABB=ON  PLU=ON  L41 AND (?CELLULOS? OR ?POLYVINYL?)
                /BI,IT
L43         127 SEA SPE=ON  ABB=ON  PLU=ON  L13 AND (PRD<20010928 OR PD<2001092
                8 OR AD<20010928)
L44         128 SEA SPE=ON  ABB=ON  PLU=ON  L13 AND (PRD<20010929 OR PD<2001092
                9 OR AD<20010929)
L45           1 SEA SPE=ON  ABB=ON  PLU=ON  L44 NOT L17
                D BIB

     FILE 'REGISTRY' ENTERED AT 13:06:58 ON 18 MAR 2010
L46          35 SEA SPE=ON  ABB=ON  PLU=ON  GELLAN GUM?/CNS
L47          35 SEA SPE=ON  ABB=ON  PLU=ON  ?GELLAN GUM?/CNS

     FILE 'USPATFULL, USPATOLD, USPAT2' ENTERED AT 13:07:25 ON 18 MAR 2010
L48        1027 SEA SPE=ON  ABB=ON  PLU=ON  L47
L49        4175 SEA SPE=ON  ABB=ON  PLU=ON  ?GELLAN GUM?/BI,IT
L50        4269 SEA SPE=ON  ABB=ON  PLU=ON  (L48 OR L49)
L51          11 SEA SPE=ON  ABB=ON  PLU=ON  L17 AND L50
                D KWIC 1-11
L52           3 SEA SPE=ON  ABB=ON  PLU=ON  L42 AND L50
L53          72 SEA SPE=ON  ABB=ON  PLU=ON  L17 AND PHARM?/BI,IT
L54          50 SEA SPE=ON  ABB=ON  PLU=ON  L24 OR L32 OR L45 OR L42 OR L51 OR
                L52
L55          79 SEA SPE=ON  ABB=ON  PLU=ON  L54 OR L19
L56          79 DUP REM L55 (0 DUPLICATES REMOVED)
                    ANSWERS '1-68' FROM FILE USPATFULL
                    ANSWERS '69-79' FROM FILE USPAT2

     FILE 'USPATFULL, USPATOLD, USPAT2' ENTERED AT 13:12:51 ON 18 MAR 2010

     FILE 'REGISTRY' ENTERED AT 13:14:30 ON 18 MAR 2010

     FILE 'USPATFULL, USPATOLD, USPAT2' ENTERED AT 13:14:56 ON 18 MAR 2010
                D STAT QUE L24
                D STAT QUE L32
                D STAT QUE L45
                D STAT QUE L42
                D STAT QUE L51
                D STAT QUE L52
                D STAT QUE L19
L57          79 SEA SPE=ON  ABB=ON  PLU=ON  L24 OR L32 OR L45 OR L42 OR L51 OR
                L52 OR L19
                D HITRN 1
                D IBIB ABS KWIC HITRN L57 1-79
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FILE HOME

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 18 Mar 2010 (20100318/PD)
FILE LAST UPDATED: 18 Mar 2010 (20100318/ED)
HIGHEST GRANTED PATENT NUMBER: US7681247
HIGHEST APPLICATION PUBLICATION NUMBER: US20100071105
CA INDEXING IS CURRENT THROUGH 18 Mar 2010 (20100318/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 Mar 2010 (20100318/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2009

USPATFULL now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

To ensure comprehensive retrieval of US patent information, including US patent application information, search USPATFULL in combination with USPAT2.

FILE USPATOLD

FILE COVERS U.S. PATENTS 1790-1975
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USPATOLD now includes complete International Patent Classification (IPC) reclassification data for the first quarter of 2010.

FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 18 Mar 2010 (20100318/PD)
FILE LAST UPDATED: 18 Mar 2010 (20100318/ED)
HIGHEST GRANTED PATENT NUMBER: US20080185484
HIGHEST APPLICATION PUBLICATION NUMBER: US20100070410
CA INDEXING IS CURRENT THROUGH 16 Mar 2010 (20100316/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 Mar 2010 (20100318/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2009

USPAT2 now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

To ensure comprehensive retrieval of US patent information, including US patent application information, search USPAT2 in combination with USPATFULL.

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file

provided by InfoChem.

STRUCTURE FILE UPDATES: 17 MAR 2010 HIGHEST RN 1211109-76-0
DICTIONARY FILE UPDATES: 17 MAR 2010 HIGHEST RN 1211109-76-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 8, 2010.

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http://www.cas.org/support/stngen/stndoc/properties.html

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